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Scientific and Technical Information Center

SEARCH REQUEST FORM

Date: 4/27/01 Requester's Full Name: Grace Hyu Examiner #: 77391
Art Unit: 1622 Phone (301) 7055 Serial Number: 09/148,973
Results Format Preferred (circle): PAPER DISK E-MAIL

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: Method of Administering An AMPA Receptor Antagonist
Inventors (please provide full names): See Attached

Earliest Priority Date: 9/4/98

Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc. if known.

For Sequence Searches Only Please include all pertinent information (parent, grandchild, divisional, or issued patent numbers) along with the appropriate serial number.

Please Search Claims 1-9

U.S. Pat. 4,899,731 for AMPA receptor Antagonist

09/148973

Push

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Searcher: Jan
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Date Searcher Picked Up: 4/30
Date Completed: 4/30
Searcher Prep & Review Time: 15
Online Time: +60

Type of Search

____ NA Sequence (#)
____ AA Sequence (#)
☒ Structure (#)
____ Bibliographic
____ Litigation
____ Fulltext
____ Other

Vendors and Cost

☒ STN _____ Dialog
____ Questel/Orbit _____ Dr. Link
____ Lexis/Nexis _____ Westlaw
____ WWW/Internet
____ In-house sequence systems (list)
____ Other (specify)

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(FILE 'HOME' ENTERED AT 16:10:22 ON 30 APR 2001)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 16:10:35 ON 30 APR 2001

L1 E GREENAMYRE J/AU
80 S E4-E10
L2 E CHENARD B/AU
73 S E4-E9
E WELCH W/AU
L3 15 S E3,E14
L4 73 S E20-E25
E MENNITI F/AU
L5 38 S E4-E7
L6 252 S L1-L5
L7 22 S L6 AND AMPA
L8 10 S L6 AND AMINO(L)HYDROXY(L)METHYL(L)ISOXAZOL?

FILE 'REGISTRY' ENTERED AT 16:14:04 ON 30 APR 2001

L9 1 S 77521-29-0

FILE 'HCAPLUS' ENTERED AT 16:14:10 ON 30 APR 2001

L10 1054 S L9
L11 2 S L6 AND L10
L12 24 S L7,L8,L11
L13 1 S L6 AND DIETHYLAMINOMETHYLPYRIDIN? (L) QUINAZOL?

FILE 'REGISTRY' ENTERED AT 16:16:00 ON 30 APR 2001

L14 1 S 59-92-7
E D-TYROSINE, 3-HYDROXY-/CN
L15 1 S E3
E DL-TYROSINE, 3-HYDROXY-/CN
L16 1 S E3
L17 1 S 28860-95-9
E C10H14N2O4/MF
L18 5 S E3 AND BENZENEPROPANOIC AND HYDRAZIN?
L19 3 S L18 NOT (ESTER OR 5 DIHYDROXY)
L20 1 S 322-35-0
E C10H15N3O5/MF
L21 5 S E3 AND 46.150.18/RID AND SERINE AND TRIHYDROXYPHENYL
L22 5 S L21 AND HYDRAZ?
L23 4 S L22 NOT 5
L24 3 S L23 NOT 4228-70-0
L25 1 S 199655-81-7
L26 1 S 199655-81-7/CRN

FILE 'HCAOLD' ENTERED AT 16:21:33 ON 30 APR 2001

L27 0 S L25 OR L26

FILE 'HCAPLUS' ENTERED AT 16:21:37 ON 30 APR 2001

L28 4 S L25 OR L26
L29 4 S L28 AND L6
L30 1 S L28 AND L10
L31 4 S L28 AND AMPA
L32 4 S L28-L31

FILE 'REGISTRY' ENTERED AT 16:23:03 ON 30 APR 2001

L33 3 S L14-L16
SEL RN
L34 95 S E1-E3/CRN
L35 3 S L17,L19
SEL RN
L36 22 S E4-E6/CRN
L37 3 S L20,L24
SEL RN

Point of Contact:
Jan Delaval
Librarian-Physical Sciences
CM1 1E01 Tel: 308-4498

L38 8 S E7-E9/CRN
 L39 7 S L34 AND L36,L38
 L40 2 S L39 AND 2/NC
 L41 7 S L38 NOT L40

FILE 'HCAPLUS' ENTERED AT 16:24:25 ON 30 APR 2001

L42 102 S L40
 L43 9797 S L33
 L44 14549 S DOPA OR LEVODOPA
 L45 15989 S L43,L44
 L46 843 S L35 OR L37
 L47 1209 S BENSERAZIDE OR CARBIDOPA
 L48 1496 S L46,L47
 L49 1085 S L45 AND L48
 L50 1127 S L42,L49
 L51 3 S L50 AND L10
 L52 6 S L50 AND AMPA
 L53 0 S L50 AND (AMINO(L)HYDROXY(L)METHYL(L)ISOXAZOL?)
 L54 6 S L51,L52
 L55 2 S L54 AND L32
 L56 2 S L31 AND L45,L48
 L57 2 S L55,L56

FILE 'REGISTRY' ENTERED AT 16:28:34 ON 30 APR 2001

L58 1 S 9042-64-2

FILE 'HCAPLUS' ENTERED AT 16:28:40 ON 30 APR 2001

L59 1 S L32 AND L58
 L60 1 S L32 AND ?DECARBOXYLASE?
 L61 4 S L32,L57,L59,L60
 L62 12 S L42 AND DYSKINES?
 L63 3 S L42 AND TREMOR?
 L64 49 S L42 AND ?PARKINSON?
 L65 4 S L42 AND (CHOREA OR BALLISM OR DYSTON? OR ATHETO? OR MYOCLONUS
 L66 6 S L42 AND MOTOR
 L67 0 S L62-L66 AND L61
 E DYSKINES/CT
 E E5+ALL
 L68 48 S E1
 L69 774 S E2
 E DYSKINES/CW
 L70 136 S E4
 L71 2 S L61 AND L68-L70
 L72 4 S L61,L71
 L73 14 S L64 AND L62,L63,L65,L66,L68-L70
 L74 16997 S NMDA
 L75 4925 S KAINIC ACID

FILE 'REGISTRY' ENTERED AT 16:37:48 ON 30 APR 2001

L76 2 S 6384-92-5 OR 487-79-6
 E L-ASPARTIC ACID, N-METHYL-/CN
 L77 1 S E3
 E DL-ASPARTIC ACID, N-METHYL-/CN
 L78 1 S E3
 E 3-PYRROLIDINEACETIC ACID, 2-CARBOXY-4-(1-METHYLETHENYL)-/CN
 L79 1 S E3
 E C10H15NO4/MF
 L80 11 S E3 AND PYRROLIDINEACETIC AND CARBOXY AND METHYLETHENYL
 L81 10 S L80 NOT T/ELS

FILE 'HCAPLUS' ENTERED AT 16:40:21 ON 30 APR 2001

L82 8562 S L76-L79,L81
 L83 11908 S N() (METHYLASPARTIC OR METHYLASPARTATE OR METHYL(1W) (ASPARTIC
 E GLUTAMATE RECEPTOR/CT
 E E5+ALL
 L84 7753 S E8+NT

L85 25779 S L74,L75,L82-L84
 L86 109 S SINEMET OR MADOPAR
 L87 137 S L42,L86
 L88 1 S L87 AND L85
 L89 0 S L87 AND (L10 OR AMPA)

FILE 'USPATFULL' ENTERED AT 16:44:15 ON 30 APR 2001
 L90 1 S L25,L26

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FILE COVERS 1947 - 30 Apr 2001 VOL 134 ISS 19
 FILE LAST UPDATED: 29 Apr 2001 (20010429/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d all hitstr tot 172

L72 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
 AN 1999:175749 HCAPLUS
 DN 130:218317
 TI **AMPA** antagonists for the treatment of dyskinesias associated with dopamine agonist therapy
 IN **Chenard, Bertrand Leo; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.**
 PA Pfizer Products Inc., USA
 SO Eur. Pat. Appl., 22 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 IC ICM A61K031-505
 ICI A61K031-505, A61K031-195, A61K031-15
 CC 1-11 (Pharmacology)
 Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900568	A2	19990310	EP 1998-307181	19980904
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 11158072	A2	19990615	JP 1998-245269	19980831
	AU 9883120	A1	19990318	AU 1998-83120	19980904
	US 6136812	A	20001024	US 1998-148974	19980904
	CA 2246839	AA	19990305	CA 1998-2246839	19980908
PRAI	US 1997-58098	P	19970905		

OS MARPAT 130:218317

AB The invention relates to a method of treating dyskinesias assocd. with dopamine agonist therapy in a mammal which comprises administering to said mammal a compd., as defined herein, which is an antagonist of the **AMPA** receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease. One example compd. of the 212 claimed was (S)-3-(2-chlorophenyl)-2-[2-(5-diethylaminomethyl-2-fluorophenyl)vinyl]-6-fluoro-3H-quinazolin-4-one.

ST **AMPA** antagonist dyskinesia dopamine agonist

IT Drug delivery systems
Parkinson's disease
(**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **AMPA** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **Dyskinesia (nervous system)**
(Parkinson's-assocd.; **AMPA** antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 51-61-6, Dopamine, biological studies 59-92-7, biological studies 322-35-0, **Benserazide** 3257-47-4
28860-95-9, Carbidopa 199655-53-3 199655-54-4
199655-56-6 199655-57-7 199655-58-8 199655-59-9 199655-61-3
199655-62-4 199655-63-5 199655-64-6 199655-65-7 199655-66-8
199655-67-9 199655-68-0 199655-69-1 199655-70-4 199655-71-5
199655-72-6 199655-75-9 199655-76-0 199655-77-1 199655-78-2
199655-80-6 **199655-81-7** 199655-82-8 199655-84-0
199655-86-2 199655-87-3 199655-88-4 199655-89-5 199655-90-8
199655-91-9 199656-00-3 199656-44-5 212710-60-6 212710-61-7
212710-62-8 212710-64-0 212710-65-1 212710-66-2 212710-70-8
212765-03-2 212850-63-0 212850-64-1 212850-72-1 212850-74-3
212850-78-7 212850-79-8 212850-80-1 212850-81-2 212850-82-3
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221167-96-0 221167-97-1 221167-99-3 221168-01-0 221168-06-5
221168-10-1 221168-22-5 221168-25-8 221168-27-0 221168-39-4
221168-41-8 221168-42-9 221168-44-1 221168-46-3 221168-49-6
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221177-89-5 221177-90-8 221177-91-9
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 77521-29-0, Ampa

RL: BSU (Biological study, unclassified); BIOL (Biological study) (antagonists; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 9042-64-2, Dopa decarboxylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 59-92-7, biological studies 322-35-0,

Benserazide 28860-95-9, Carbidopa

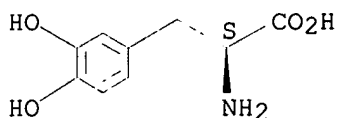
199655-81-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 59-92-7 HCAPLUS

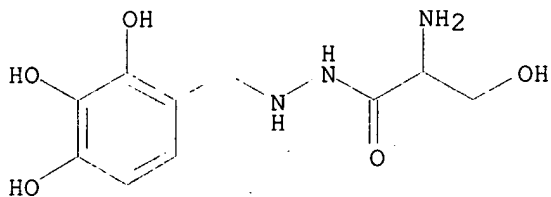
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 322-35-0 HCAPLUS

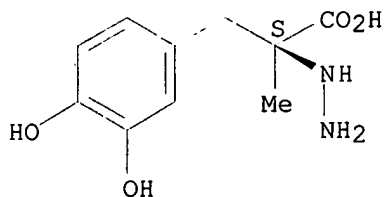
CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)



RN 28860-95-9 HCAPLUS

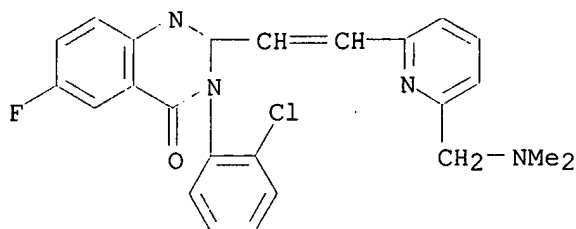
CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 199655-81-7 HCAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)

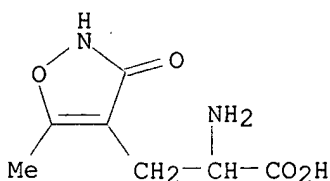


IT 77521-29-0, Ampa

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; **AMPA** antagonists for treatment of dyskinesias
assocd. with dopamine agonist therapy)

RN 77521-29-0 HCAPLUS

CN 4-Isioxazolepropanoic acid, .alpha.-amino-2,3-dihydro-5-methyl-3-oxo- (9CI)
(CA INDEX NAME)



IT 9042-64-2, Dopa decarboxylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **AMPA** antagonists for treatment of dyskinesias
assocd. with dopamine agonist therapy)

RN 9042-64-2 HCAPLUS

CN Decarboxylase, aromatic amino acid (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L72 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:175748 HCAPLUS

DN 130:209717

TI Preparation of 3-(2-chlorophenyl)-2-[2-(6-diethylaminomethylpyridin-2-yl)vinyl]-6-fluoro-3H-quinazolin-4-one as an **AMPA** antagonist for the treatment of dyskinesias associated with dopamine agonist therapy.

IN **Chenard, Bertrand Leo; Greenamyre, John Timothy; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.**

PA Pfizer Products Inc., USA

SO Eur. Pat. Appl., 6 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K031-505

ICI A61K031-505, A61K031-195, A61K031-15

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

FAN.CNT 1

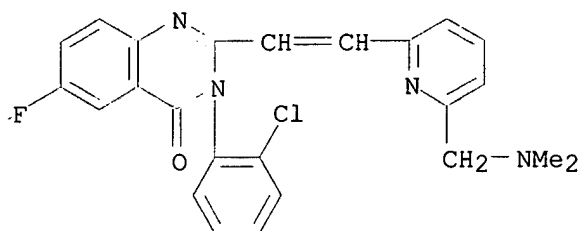
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900567	A2	19990310	EP 1998-306661	19980820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2246560	AA	19990305	CA 1998-2246560	19980903
	JP 11139991	A2	19990525	JP 1998-249644	19980903
	AU 9883193	A1	19990318	AU 1998-83193	19980907
PRAI	US 1997-57965		19970905		
AB	A method for the treatment of dyskinesias assocd. with dopamine agonist therapy comprising administration of an AMPA antagonist is				

- claimed (no data). Thus, 3-(2-chlorophenyl)-6-fluoro-2-methyl-4-(3H)-quinazolinone (prepn. given) was refluxed with 2,6-pyridinedicarboxaldehyde, ZnCl₂, and Ac₂O in dioxane to give 33% 6-[2-[3-(2-chlorophenyl)-6-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl]vinyl]pyridine-2-carboxaldehyde. This was stirred with Et₂NH and NaBH(AcO)₃ in CH₂Cl₂ to give 24% title compd. as the monomaleate salt.
- ST chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone prepn
AMPA antagonist; quinazolinone chlorophenyldiethylaminomethylpyridinylvinyl prepn **AMPA** antagonist; dyskinesia treatment
AMPA antagonist chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone
- IT **AMPA** receptors
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
 (antagonists; prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT **Dyskinesia (nervous system)**
 (treatment; prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT **220931-86-2P**
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT **199655-81-7**
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT **59-92-7, L-Dopa, miscellaneous 322-35-0, Benserazide 28860-95-9, Carbidopa**
 RL: MSC (Miscellaneous)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 95-51-2, 2-Chloroaniline 109-89-7, reactions 320-98-9 5431-44-7, 2,6-Pyridinedicarboxaldehyde
 RL: RCT (Reactant)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT 38520-78-4P 49579-12-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- IT **220931-86-2P**
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)
- RN 220931-86-2 HCAPLUS
 CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 199655-81-7

CMF C24 H20 Cl F N4 O



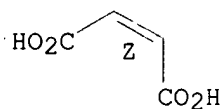
CM 2

CRN 110-16-7

CMF C4 H4 O4

CDIS 2:2

Double bond geometry as shown.



IT 199655-81-7

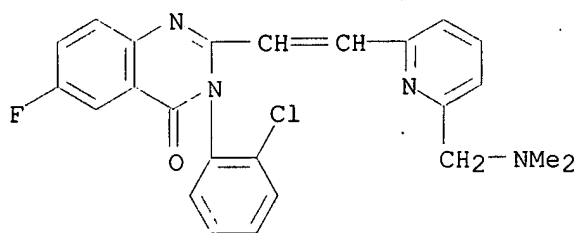
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 199655-81-7 HCAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)

IT 59-92-7, L-Dopa, miscellaneous 322-35-0,
Benserazide 28860-95-9, Carbidopa

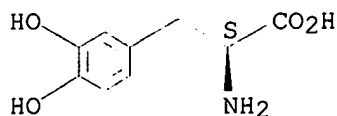
RL: MSC (Miscellaneous)

(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an **AMPA** antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

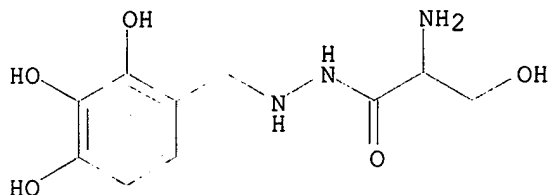
RN 59-92-7 HCAPLUS

CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

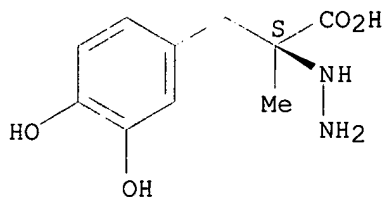


RN 322-35-0 HCAPLUS
 CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)



RN 28860-95-9 HCAPLUS
 CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-,
 (.alpha.S)- (9CI) (CA INDEX NAME)

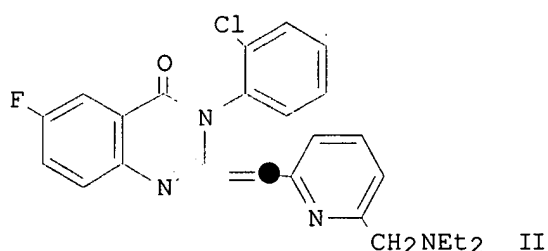
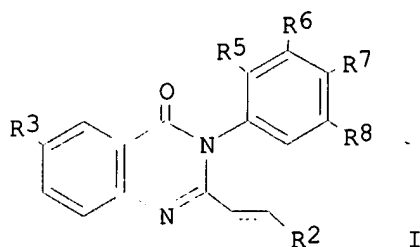
Absolute stereochemistry.



L72 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
 AN 1998:608605 HCAPLUS
 DN 129:230733
 TI Preparation of atropisomers of 3-aryl-4(3H)-quinazolinones and their use
 as AMPA-receptor antagonists
 IN Welch, Willard McKowan, Jr.; Devries, Keith M.
 PA Pfizer Products Inc., USA
 SO PCT Int. Appl., 81 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D239-91
 ICS C07D401-06; C07D417-06; C07D401-14; C07D405-06; C07D413-06;
 A61K031-505; C07M007-00
 CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
 Section cross-reference(s): 1, 63
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9838173	A1	19980903	WO 1998-IB150	19980206
W:			AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG	
AU 9856768	A1	19980918	AU 1998-56768	19980206
EP 968194	A1	20000105	EP 1998-900978	19980206
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO	
BR 9807872	A	20000321	BR 1998-7872	19980206
JP 2000509731	T2	20000802	JP 1998-537448	19980206
NO 9904177	A	19990827	NO 1999-4177	19990827
PRAI US 1997-38905	P	19970228		
WO 1998-IB150	W	19980206		

OS MARPAT 129:230733
GI



AB Title atropisomers [I; wherein R2 is an optionally substituted aryl or heteroaryl, R5 is alkyl, halo, CF3, alkoxy or alkylthio, R6, R7 and R8 are hydrogen or halo, and R3 is hydrogen, halo, CN, NO2, CF3, alkyl or alkoxy] are prepd. and are useful as **AMPA** receptor antagonists, particularly in the treatment of neurodegenerative and CNS-trauma related conditions (no data). The title (S)-atropisomer II was prepd. from 2-chloroaniline, 6-fluoro-2-methylquinoxalin-4-one which was prepd. from hydrogenation, acetylation, and cyclization of 2-nitro-5-fluorobenzoic acid, followed by reaction with 2,6-pyridinedicarboxaldehyde, and diethylamine, and was column sepd.

ST quinazolinone prepn; atropisomer quinazolinone sepn HPLC receptor antagonist

IT Separation
(HPLC column; prepn. and sepn. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT **AMPA** receptors
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antagonists; prepn. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT	212850-63-0P	212850-64-1P	212850-65-2P	212850-66-3P	212850-68-5P
	212850-70-9P	212850-72-1P	212850-73-2P	212850-74-3P	212850-75-4P
	212850-76-5P	212850-77-6P	212850-78-7P	212850-79-8P	212850-80-1P
	212850-81-2P	212850-82-3P	212916-59-1P	212916-60-4P	212916-61-5P
	212916-62-6P	212916-63-7P	212916-64-8P	212916-65-9P	

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of atropisomers of arylquinazolinones as **AMPA**-receptor antagonists)

IT 95-51-2, 2-Chloroaniline 109-89-7, Diethylamine, reactions 320-98-9
340-57-8 617-84-5, Diethylformamide 626-05-1, 2,6-Dibromopyridine
5431-44-7, 2,6-Pyridinedicarboxaldehyde 20949-84-2 27366-72-9
49579-01-3 49579-08-0 199656-43-4
RL: RCT (Reactant)

(prepn. of atropisomers of arylquinazolinones as **AMPA**
-receptor antagonists)

IT 10200-43-8P 49579-12-6P 68683-04-5P 78441-69-7P 82586-66-1P
 113732-84-6P 141567-53-5P 174608-36-7P 194473-04-6P 199599-68-3P
 199655-35-1P 199655-36-2P 199655-54-4P 199655-55-5P 199655-57-7P
 199655-61-3P 199655-62-4P 199655-63-5P 199655-65-7P 199655-66-8P
 199655-67-9P 199655-68-0P 199655-69-1P 199655-70-4P 199655-71-5P
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199655-81-7P 199655-82-8P 199655-83-9P 199655-84-0P
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 199655-91-9P 199655-92-0P 199655-93-1P 199655-96-4P 199655-97-5P
 199655-98-6P 199655-99-7P 199656-02-5P 199656-03-6P 199656-04-7P
 199656-05-8P 199656-06-9P 199656-28-5P 199656-29-6P 199656-30-9P
 199656-31-0P 199656-32-1P 199656-33-2P 199656-34-3P 199656-35-4P
 199656-40-1P 212764-92-6P 212764-93-7P 212764-94-8P 212764-95-9P
 212764-96-0P 212764-97-1P 212764-99-3P 212765-00-9P 212765-01-0P
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 212765-13-4P 212765-15-6P 212765-16-7P 212765-19-0P 212765-20-3P
 212765-21-4P 212765-22-5P 212765-23-6P 212765-24-7P 212765-25-8P
 212765-26-9P 212765-27-0P 212765-28-1P 212772-14-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of atropisomers of arylquinazolinones as **AMPA**
-receptor antagonists)

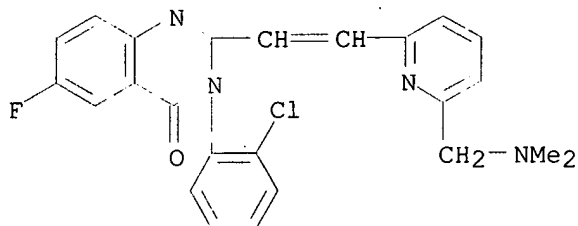
IT **199655-81-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of atropisomers of arylquinazolinones as **AMPA**
-receptor antagonists)

RN 199655-81-7 HCAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



L72 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS

AN 1997:752948 HCAPLUS

DN 128:34774

TI Preparation of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA**
receptor antagonists.

IN Elliott, Mark Leonard; Welch, Willard Mckowan Jr

PA Pfizer Inc., USA; Elliott, Mark Leonard; Welch, Willard Mckowan Jr.

SO PCT Int. Appl., 77 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D401-06

ICS C07D401-04; C07D401-14; C07D405-06; C07D403-06; C07D239-91;

C07D417-14; C07D417-06; A61K031-505

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

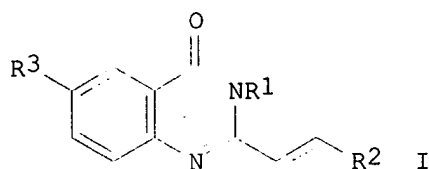
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743276	A1	19971120	WO 1997-IB134	19970217
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
 RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
 YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
 MR, NE, SN, TD, TG

CA 2252907 AA 19971120 CA 1997-2252907 19970217
 AU 9715549 A1 19971205 AU 1997-15549 19970217
 EP 901487 A1 19990317 EP 1997-901749 19970217
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
 SI, LT, LV, FI, RO
 CN 1218464 A 19990602 CN 1997-194654 19970217
 BR 9709085 A 19990803 BR 1997-9085 19970217
 JP 11514663 T2 19991214 JP 1997-540682 19970217
 ZA 9704156 A 19981116 ZA 1997-4156 19970514
 NO 9805293 A 19990113 NO 1998-5293 19981113
 PRAI US 1996-17738 19960515
 WO 1997-IB134 19970217
 OS MARPAT 128:34774
 GI



AB Title compds. [I; R1 = (substituted) Ph, pyridyl; R2 = (substituted) Ph, 5-6 membered heterocyclyl; R3 = H, halo, cyano, No2, CF3, alkyl, alkoxy], were prepd. Thus, 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylvinyl)-3H-quinazolin-4-one was hydrogenated in EtOAc over Pd/C to give 100% 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylethyl)-3H-quinazolin-4-one. Tested I inhibited **AMPA** receptor activation-induced 45Ca^{2+} uptake with $\text{IC}_{50} < 5 \mu\text{M}$.

ST quinazolinone prepn **AMPA** receptor antagonist; nervous system agents quinazolinone

IT Nervous system agents

Neurotransmitter antagonists

(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT	3257-47-4P	199655-35-1P	199655-36-2P	199655-37-3P	199655-38-4P
	199655-39-5P	199655-40-8P	199655-41-9P	199655-42-0P	199655-43-1P
	199655-44-2P	199655-45-3P	199655-46-4P	199655-47-5P	199655-48-6P
	199655-49-7P	199655-50-0P	199655-51-1P	199655-52-2P	199655-53-3P
	199655-54-4P	199655-55-5P	199655-56-6P	199655-57-7P	199655-58-8P
	199655-59-9P	199655-60-2P	199655-61-3P	199655-62-4P	199655-63-5P
	199655-64-6P	199655-65-7P	199655-66-8P	199655-67-9P	199655-68-0P
	199655-69-1P	199655-70-4P	199655-71-5P	199655-72-6P	199655-73-7P
	199655-74-8P	199655-75-9P	199655-76-0P	199655-77-1P	199655-78-2P
	199655-79-3P	199655-80-6P	199655-81-7P	199655-82-8P	
	199655-83-9P	199655-84-0P	199655-85-1P	199655-86-2P	199655-87-3P
	199655-88-4P	199655-89-5P	199655-90-8P	199655-91-9P	199655-92-0P
	199655-93-1P	199655-94-2P	199655-95-3P	199655-96-4P	199655-97-5P
	199655-98-6P	199655-99-7P	199656-00-3P	199656-01-4P	199656-02-5P
	199656-03-6P	199656-04-7P	199656-05-8P	199656-06-9P	199656-07-0P
	199656-08-1P	199656-09-2P	199656-10-5P	199656-11-6P	199656-12-7P
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	199656-18-3P	199656-19-4P	199656-20-7P	199656-21-8P	199656-22-9P
	199656-23-0P	199656-24-1P	199656-25-2P	199656-26-3P	199656-27-4P

199656-28-5P 199656-29-6P 199656-30-9P 199656-31-0P 199656-32-1P
 199656-33-2P 199656-34-3P 199656-35-4P 199656-36-5P 199656-37-6P
 199656-38-7P 199656-39-8P 199656-40-1P 199656-41-2P 199656-44-5P
 199656-45-6P 199656-46-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 95-51-2, 2-Chloroaniline 320-98-9 340-57-8 5431-44-7,
 2,6-Pyridinedicarboxaldehyde 20949-84-2, 2-Methylthiazole-4-
 carboxaldehyde 49579-01-3 49579-08-0 199599-68-3 199656-42-3
 199656-43-4

RL: RCT (Reactant)

(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

IT 38520-78-4P 49579-12-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

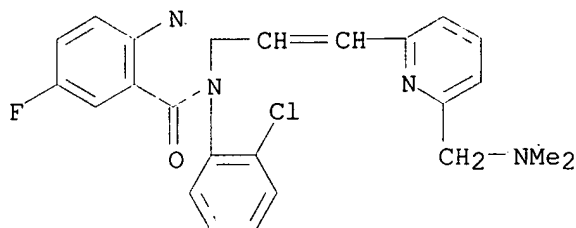
IT 199655-81-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as **AMPA** receptor antagonists)

RN 199655-81-7 HCAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> fil uspatful

FILE 'USPATFULL' ENTERED AT 16:45:05 ON 30 APR 2001

CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 24 Apr 2001 (20010424/PD)

FILE LAST UPDATED: 24 Apr 2001 (20010424/ED)

HIGHEST PATENT NUMBER: US6223348

CA INDEXING IS CURRENT THROUGH 24 Apr 2001 (20010424/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 24 Apr 2001 (20010424/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2000

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Oct 2000

>>> Page images are available for patents from 1/1/1997. Current <<<
 >>> week patent text is typically loaded by Thursday morning and <<<
 >>> page images are available for display by the end of the day. <<<
 >>> Image data for the /FA field are available the following week. <<<

>>> Complete CA file indexing for chemical patents (or equivalents) <<<
 >>> is included in file records. A thesaurus is available for the <<<
 >>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<<
 >>> fields. This thesaurus includes catchword terms from the <<<
 >>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<
 >>> available for the WIPO International Patent Classification <<<

>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<
>>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<
>>> the /IC5 and /IC fields include the corresponding catchword <<<
>>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d bib abs hitstr 190

L90 ANSWER 1 OF 1 USPATFULL
AN 2000:142378 USPATFULL
TI Methods of administering AMPA receptor antagonists to treat dyskinesias associated with dopamine agonist therapy
IN Chenard, Bertrand L., Waterford, CT, United States
Welch, Willard M., Mystic, CT, United States
Menniti, Frank S., Mystic, CT, United States
PA Pfizer Inc, New York, NY, United States (U.S. corporation)
PI US 6136812 20001024
AI US 1998-148974 19980904 (9)
PRAI US 1997-58098 19970905 (60)
DT Utility
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Richardson, Peter C.; Ginsberg, Paul H.; Konstas, Kristina L.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2016

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to a method of treating dyskinesias associated with dopamine agonist therapy in a mammal which comprises administering to said mammal a compound, as defined herein, which is an antagonist of the AMPA receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease.

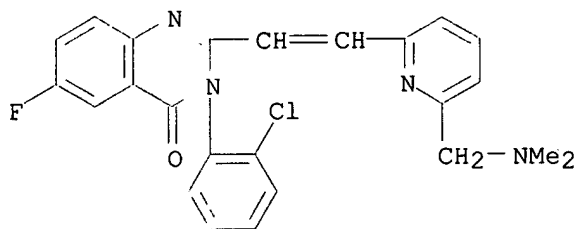
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 199655-81-7

(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 199655-81-7 USPATFULL

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> fil reg

FILE 'REGISTRY' ENTERED AT 16:45:26 ON 30 APR 2001

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 29 APR 2001 HIGHEST RN 333381-38-7

DICTIONARY FILE UPDATES: 29 APR 2001 HIGHEST RN 333381-38-7

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

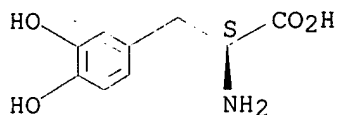
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

=> d ide can l14

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 59-92-7 REGISTRY
CN L-Tyrosine, 3-hydroxy- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Alanine, 3-(3,4-dihydroxyphenyl)-, L- (8CI)
OTHER NAMES:
CN (-)-3,4-Dihydroxyphenylalanine
CN (-)-Dopa
CN .beta.-(3,4-Dihydroxyphenyl)-.alpha.-L-alanine
CN .beta.-(3,4-Dihydroxyphenyl)-L-alanine
CN .beta.-(3,4-Dihydroxyphenyl)alanine
CN 3,4-Dihydroxy-L-phenylalanine
CN 3,4-Dihydroxyphenyl-L-alanine
CN 3,4-Dihydroxyphenylalanine
CN 3-(3,4-Dihydroxyphenyl)-L-alanine
CN 3-Hydroxy-L-tyrosine
CN DA
CN Dihydroxy-L-phenylalanine
CN DOPA
CN Dopaflex
CN Dopalina
CN Dopar
CN Dopaston
CN Dopaston SE
CN Eldopal
CN Helfo-dopa
CN Insulamina
CN L-(-)-Dopa
CN L-.beta.-(3,4-Dihydroxyphenyl)-.alpha.-alanine
CN L-3-(3,4-Dihydroxyphenyl)alanine
CN L-4,5-Dihydroxyphenylalanine
CN L-DOPA
CN Larodopa
CN Levodopa
CN Levopa
CN Pardopa
FS STEREOSEARCH
DR 25525-15-9, 23734-74-9, 72572-99-7, 72573-00-3, 90638-38-3, 88250-23-1,
34241-25-3
MF C9 H11 N O4
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU,
EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE,
MRCK*, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXLINE,
TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



9109 REFERENCES IN FILE CA (1967 TO DATE)
 260 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 9123 REFERENCES IN FILE CAPLUS (1967 TO DATE)
 17 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:265967
 REFERENCE 2: 134:265203
 REFERENCE 3: 134:262181
 REFERENCE 4: 134:261267
 REFERENCE 5: 134:261182
 REFERENCE 6: 134:251260
 REFERENCE 7: 134:249755
 REFERENCE 8: 134:249215
 REFERENCE 9: 134:247378
 REFERENCE 10: 134:242762

=> d ide can 117

L17 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 28860-95-9 REGISTRY

CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-,
 (.alpha.S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-,
 (S)-

CN Hydrocinnamic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, L-
 (8CI)

OTHER NAMES:

CN (-)-L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylhydrocinnamic acid

CN (-)-L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylhydrocinnamic acid
 monohydrate

CN .alpha.-Hydrazino-.alpha.-methyl-.beta.-(3,4-dihydroxyphenyl)propionic
 acid

CN .alpha.-Methyldopahydrazine

CN 1-.alpha.-(3,4-Dihydroxybenzyl)-.alpha.-hydrazinopropionic acid

CN Carbidopa

CN Hydrazino-.alpha.-methyldopa

CN L-.alpha.-(3,4-Dihydroxybenzyl)-.alpha.-hydrazinopropionic acid

CN L-.alpha.-Hydrazino-.alpha.-methyl-.beta.-(3,4-dihydroxyphenyl)propionic
 acid

CN L-.alpha.-Hydrazino-.alpha.-methyl-3,4-dihydroxyphenylpropionic acid

CN L-.alpha.-Hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid

CN L-.alpha.-Methyl-.alpha.-hydrazino-.beta.-(3,4-dihydroxyphenyl)propionic
 acid

CN L-.alpha.-Methyl-.alpha.-hydrazino-3,4-dihydroxyphenylpropionic acid

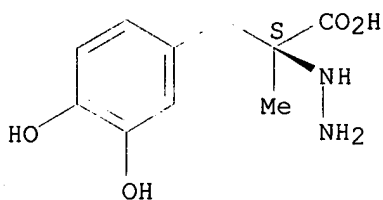
CN L-.alpha.-Methyl-.beta.-(3,4-dihydroxyphenyl)-.alpha.-hydrazinopropionic
 acid

CN L-.alpha.-Methyldopahydrazine

CN L-3-(3,4-Dihydroxyphenyl)-2-methyl-2-hydrazinopropionic acid

CN MK 486
 CN N-Aminomethyl dopa
 FS STEREOSEARCH
 DR 27925-91-3, 31823-41-3
 MF C10 H14 N2 O4
 CI COM
 LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
 BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,
 CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MRCK*,
 NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: EINECS**, WHO
 (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



540 REFERENCES IN FILE CA (1967 TO DATE)
 7 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 541 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:256873
 REFERENCE 2: 134:242762
 REFERENCE 3: 134:198100
 REFERENCE 4: 134:188216
 REFERENCE 5: 134:172697
 REFERENCE 6: 134:168355
 REFERENCE 7: 134:157584
 REFERENCE 8: 134:157063
 REFERENCE 9: 134:121022
 REFERENCE 10: 134:120931

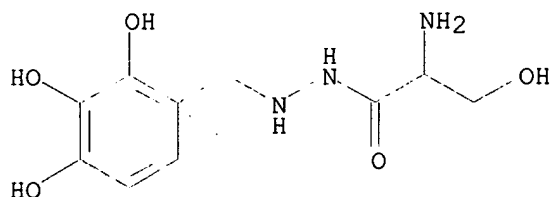
=> d ide can 120

L20 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
 RN 322-35-0 REGISTRY
 CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN DL-Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide
 CN Serine, 2-(2,3,4-trihydroxybenzyl)hydrazide (7CI)
 CN Serine, 2-(2,3,4-trihydroxybenzyl)hydrazide, DL- (8CI)
 OTHER NAMES:
 CN Benserazide
 CN DL-Seryltrihydroxybenzylhydrazine
 CN N-(DL-Seryl)-N'-(2,3,4-trihydroxybenzyl)hydrazine
 CN N1-(DL-Seryl)-N2-(2,3,4-trihydroxybenzyl)hydrazine
 CN N1-(DL-Seryl)-N2-(2,3,4-trihydroxybenzyl)hydrazine hydrochloride
 CN Serazide

MF C10 H15 N3 O5

CI COM

LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDb, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



346 REFERENCES IN FILE CA (1967 TO DATE)

5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

347 REFERENCES IN FILE CAPLUS (1967 TO DATE)

20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:249866

REFERENCE 2: 134:188216

REFERENCE 3: 134:105933

REFERENCE 4: 134:95504

REFERENCE 5: 134:3509

REFERENCE 6: 133:325730

REFERENCE 7: 133:256811

REFERENCE 8: 133:227909

REFERENCE 9: 133:183136

REFERENCE 10: 133:182991

=> d ide can 140 tot

L40 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS

RN 57308-51-7 REGISTRY

CN L-Tyrosine, 3-hydroxy-, mixt. with (.alpha.S)-.alpha.-hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (S)-, mixt. contg.

CN Benzenepropanoic acid, .alpha.-hydrazino-3,4-dihydroxy-.alpha.-methyl-, (.alpha.S)-, mixt. contg. (9CI)

CN L-Tyrosine, 3-hydroxy-, mixt. with (S)-.alpha.-hydrazino-3,4-dihydroxy-.alpha.-methylbenzenepropanoic acid

OTHER NAMES:

CN Carbidopa-L-dopa mixt.

CN Carbidopa-levodopa mixt.

CN Isicom

CN Nacom

CN Nakom

CN Sinemet

FS STEREOSEARCH

MF C10 H14 N2 O4 . C9 H11 N O4

CI MXS

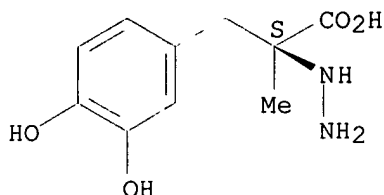
LC STN Files: BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB,
 CEN, CIN, DIOGENES, EMBASE, IMSDIRECTORY, MEDLINE, MRCK*, PROMT, RTECS*,
 TOXLINE, TOXLIT, USPATFULL
 (*File contains numerically searchable property data)

CM 1

CRN 28860-95-9

CMF C10 H14 N2 O4

Absolute stereochemistry.

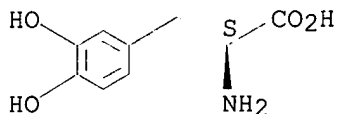


CM 2

CRN 59-92-7

CMF C9 H11 N O4

Absolute stereochemistry.



76 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

76 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:294727

REFERENCE 2: 133:204797

REFERENCE 3: 133:8986

REFERENCE 4: 131:165329

REFERENCE 5: 130:320759

REFERENCE 6: 130:261969

REFERENCE 7: 129:339741

REFERENCE 8: 129:301201

REFERENCE 9: 129:38404

REFERENCE 10: 128:212698

L40 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS

RN 37270-69-2 REGISTRY

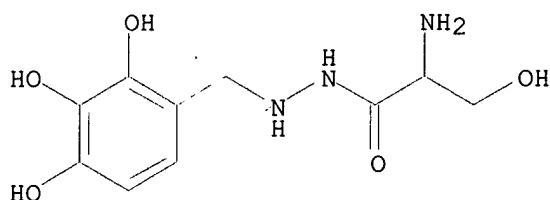
CN L-Tyrosine, 3-hydroxy-, mixt. with serine 2-[(2,3,4-
 trihydroxyphenyl)methyl]hydrazide (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN DL-Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, mixt. contg.
 CN L-Tyrosine, 3-hydroxy-, mixt. with DL-serine 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide
 CN Serine, 2-[(2,3,4-trihydroxyphenyl)methyl]hydrazide, mixt. contg. (9CI)
 OTHER NAMES:
 CN Madopar
 CN Ro 8-0576
 FS STEREOSEARCH
 DR 61949-25-5
 MF C10 H15 N3 O5 . C9 H11 N O4
 CI MXS
 LC STN Files: BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CIN, EMBASE, IMSDIRECTORY, MEDLINE, MRCK*, PROMT, TOXLINE, TOXLIT, USPATFULL
 (*File contains numerically searchable property data)

CM 1

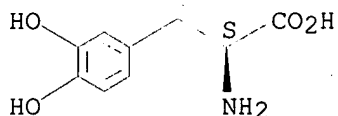
CRN 322-35-0
 CMF C10 H15 N3 O5



CM 2

CRN 59-92-7
 CMF C9 H11 N O4

Absolute stereochemistry.

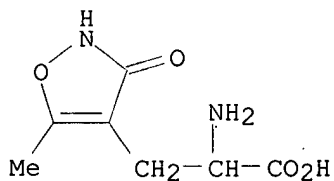


33 REFERENCES IN FILE CA (1967 TO DATE)
 33 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:294727
 REFERENCE 2: 131:266533
 REFERENCE 3: 130:7366
 REFERENCE 4: 129:239731
 REFERENCE 5: 127:272715
 REFERENCE 6: 124:250675
 REFERENCE 7: 123:275785
 REFERENCE 8: 123:74239
 REFERENCE 9: 123:782
 REFERENCE 10: 122:96274

=> d ide can 19

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 77521-29-0 REGISTRY
CN 4-Isioxazolepropanoic acid, .alpha.-amino-2,3-dihydro-5-methyl-3-oxo- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
CN (R,S)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
CN (RS)-.alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
CN .alpha.-Amino-2,3-dihydro-5-methyl-3-oxoisoxazole-4-propionic acid
CN .alpha.-Amino-3-hydroxy-5-methyl-4-isoxazolepropionate
CN .alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
CN .gamma.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
CN AMPA
CN AMPA (pharmaceutical)
CN D,L-.alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
CN dl-.alpha.-Amino-3-hydroxy-5-methylisoxazole-4-propionic acid
FS 3D CONCORD
DR 126632-03-9, 133481-32-0, 139261-99-7, 139559-02-7, 74341-63-2,
78729-80-3, 79697-77-1, 85506-19-0, 86495-63-8, 83354-19-2, 81323-87-7,
92614-50-1, 110592-37-5
MF C7 H10 N2 O4
CI COM
LC STN Files: BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT,
CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE,
MEDLINE, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)



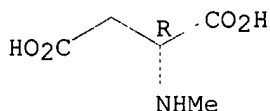
982 REFERENCES IN FILE CA (1967 TO DATE)
8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
982 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:264542
REFERENCE 2: 134:264541
REFERENCE 3: 134:202979
REFERENCE 4: 134:202883
REFERENCE 5: 134:190909
REFERENCE 6: 134:174165
REFERENCE 7: 134:173334
REFERENCE 8: 134:159650
REFERENCE 9: 134:158014
REFERENCE 10: 134:158002

=> d ide can 176 tot

L76 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2001 ACS
 RN 6384-92-5 REGISTRY
 CN D-Aspartic acid, N-methyl- (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN Aspartic acid, N-methyl-, D- (8CI)
 OTHER NAMES:
 CN N-Methyl-D-aspartic acid
 CN NMDA
 FS STEREOSEARCH
 MF C5 H9 N O4
 CI COM
 LC STN Files: AGRICOLA, AIDSLINE, BEILSTEIN*, BIOBUSINESS, BIOSIS,
 BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX,
 CHEMLIST, CIN, CSChem, EMBASE, IFICDB, IFIUDb, IPA, MEDLINE, MRCK*,
 NIOSHTIC, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
 (*File contains numerically searchable property data)

Absolute stereochemistry.



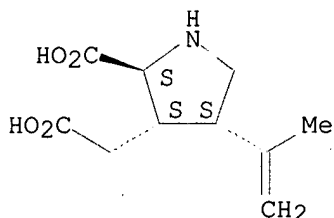
5598 REFERENCES IN FILE CA (1967 TO DATE)
 9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 5603 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:264535
 REFERENCE 2: 134:264523
 REFERENCE 3: 134:264120
 REFERENCE 4: 134:248974
 REFERENCE 5: 134:247465
 REFERENCE 6: 134:247458
 REFERENCE 7: 134:232180
 REFERENCE 8: 134:232146
 REFERENCE 9: 134:232134
 REFERENCE 10: 134:232120

L76 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2001 ACS
 RN 487-79-6 REGISTRY
 CN 3-Pyrrolidineacetic acid, 2-carboxy-4-(1-methylethenyl)-, (2S,3S,4S)-
 (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 3-Pyrrolidineacetic acid, 2-carboxy-4-(1-methylethenyl)-,
 [2S-(2.alpha.,3.beta.,4.beta.)]-
 CN 3-Pyrrolidineacetic acid, 2-carboxy-4-isopropenyl- (6CI, 7CI, 8CI)
 OTHER NAMES:
 CN (-)-.alpha.-Kainic acid
 CN (-)-Kainic acid
 CN (2S,3S,4S)-2-Carboxy-4-isopropenylpyrrolidine-3-acetic acid
 CN .alpha.-Kainic acid

CN Digenic acid
 CN Digenin
 CN Helminal
 CN Kainic acid
 CN L-.alpha.-Kainic acid
 FS STEREOSEARCH
 DR 4071-38-9, 46398-96-3
 MF C10 H15 N O4
 CI COM
 LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HODOC*, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
 (*File contains numerically searchable property data)
 Other Sources: WHO

Absolute stereochemistry. Rotation (-).



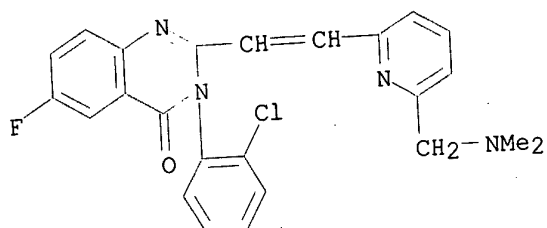
3858 REFERENCES IN FILE CA (1967 TO DATE)
 41 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 3863 REFERENCES IN FILE CAPLUS (1967 TO DATE)
 26 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:264545
 REFERENCE 2: 134:261996
 REFERENCE 3: 134:235967
 REFERENCE 4: 134:232143
 REFERENCE 5: 134:232142
 REFERENCE 6: 134:232141
 REFERENCE 7: 134:232100
 REFERENCE 8: 134:222008
 REFERENCE 9: 134:220893
 REFERENCE 10: 134:218095

=> d ide can 125

L25 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
 RN 199655-81-7 REGISTRY
 CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C24 H20 Cl F N4 O
 CI COM
 SR CA
 LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

hsu - 09 / 148973



4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

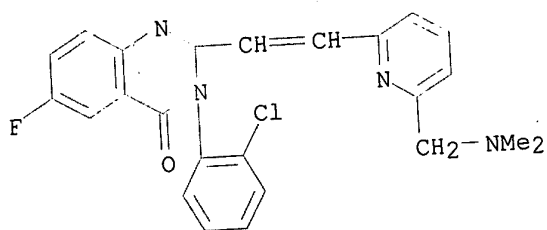
REFERENCE 1: 130:218317
REFERENCE 2: 130:209717
REFERENCE 3: 129:230733
REFERENCE 4: 128:34774

=> d ide can 126

L26 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
RN 220931-86-2 REGISTRY
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H20 Cl F N4 O . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS

CM 1

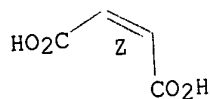
CRN 199655-81-7
CMF C24 H20 Cl F N4 O



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:209717

=> fil embase

FILE 'EMBASE' ENTERED AT 16:57:13 ON 30 APR 2001

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FILE COVERS 1974 TO 19 Apr 2001 (20010419/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his 191-

(FILE 'HCAPLUS' ENTERED AT 16:44:40 ON 30 APR 2001)

FILE 'USPATFULL' ENTERED AT 16:45:05 ON 30 APR 2001

FILE 'REGISTRY' ENTERED AT 16:45:26 ON 30 APR 2001

FILE 'EMBASE' ENTERED AT 16:48:07 ON 30 APR 2001

L91 2635 S L9
L92 2635 S ALPHA AMINO 3 HYDROXY 5 METHYL 4 ISOXAZOLEPROPIONIC ACID/CT
L93 5086 S L91,L92 OR AMPA
L94 0 S L25 OR L26
L95 2291 S L40
L96 1807 S CARBIDOPA PLUS LEVODOPA/CT
L97 928 S BENSERAZIDE PLUS LEVODOPA/CT
L98 1679 S SINEMET OR MADOPAR
L99 3 S L93 AND L95-L98
L100 19733 S L14-L16
L101 1913 S LEVODOPA(L)CB/CT
L102 3422 S L17-L19
L103 951 S CARBIDOPA(L)CB/CT
L104 2216 S L20,L24
L105 472 S BENSERAZIDE(L)CB/CT
L106 1178 S L101 AND L103,L105
L107 3 S L106 AND L93
L108 6 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE
L109 7 S L99,L107,L108
E AMPA RECEPTOR ANTAGONIST/CT
E E3+ALL
L110 5732 S E5+NT
L111 33 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE
L112 9 S (L100 OR LEVODOPA/CT) AND (L102 OR CARBIDOPA/CT OR L104 OR BE
L113 10 S L109,L112

FILE 'EMBASE' ENTERED AT 16:57:13 ON 30 APR 2001

=> d all tot 1113

L113 ANSWER 1 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 2000150429 EMBASE

TI AMPA receptor blockade improves levodopa-induced dyskinesia in MPTP monkeys.

AU Konitsiotis S.; Blanchet P.J.; Verhagen L.; Lamers E.; Chase T.N.

CS Dr. T.N. Chase, Experimental Therapeutics Branch, Building 10, Natl. Inst. Neurol. Disorders/Stroke, Bethesda, MD 20892-1406, United States.
chase@helix.nih.gov

SO Neurology, (2000) 54/8 (1589-1595).

Refs: 49

ISSN: 0028-3878 CODEN: NEURAI

CY United States
 DT Journal; Article
 FS 008 Neurology and Neurosurgery
 037 Drug Literature Index

LA English

SL English

AB Objective: To evaluate the contribution of amino-3-hydroxy-5-methyl-4-isoxazole proprionic acid (AMPA) glutamate receptors to the pathogenesis of parkinsonian signs and levodopa-induced dyskinesias. Background: Motor fluctuations and dyskinesias reflect, in part, altered function of glutamate receptors of the NMDA subtype. The possible role of AMPA receptors, however, has not yet been examined. Methods: The authors compared the ability of an AMPA agonist (CX516) and a noncompetitive AMPA antagonist (LY300164) to alter parkinsonian symptoms and levodopa-induced dyskinesia in MPTP-lesioned monkeys. Eight levodopa-treated parkinsonian monkeys received rising doses of each drug, first in monotherapy and then in combination with low-, medium-, and high-dose levodopa. Results: CX516 alone, as well as when combined with low-dose levodopa, did not affect motor activity but induced dyskinesia. Moreover, following injection of the higher doses of levodopa, it increased levodopa-induced dyskinesia by up to 52% ($p < 0.05$). LY300164 potentiated the motor activating effects of low-dose levodopa, increasing motor activity by as much as 86% ($p < 0.05$), and that of medium-dose levodopa as much as 54% ($p < 0.05$). At the same time, LY300164 decreased levodopa-induced dyskinesia by up to 40% ($p < 0.05$). Conclusions: AMPA receptor upregulation may contribute to the expression of levodopa-induced dyskinesia. Conceivably, noncompetitive AMPA receptor antagonists could be useful, alone or in combination with NMDA antagonists, in the treatment of PD, by enhancing the antiparkinsonian effects of levodopa without increasing and possibly even decreasing levodopa-induced dyskinesia.

CT Medical Descriptors:

*dyskinesia: PC, prevention
 *Parkinson disease: PC, prevention
 pathogenesis
 monkey
 dose response
 receptor upregulation
 receptor blocking
 combination chemotherapy
 disease severity
 nonhuman
 male
 female
 animal model
 controlled study
 animal tissue
 animal cell
 article
 priority journal

Drug Descriptors:

*AMPA receptor agonist: PD, pharmacology
 *AMPA receptor agonist: SC, subcutaneous drug administration
 *AMPA receptor antagonist: CB, drug combination
 *AMPA receptor antagonist: PD, pharmacology
 *AMPA receptor antagonist: SC, subcutaneous drug administration
 *levodopa: PD, pharmacology
 *n methyl dextro aspartic acid receptor blocking agent: CB, drug combination
 *n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
 6 quinoxalinecarboxylic acid piperidide: PD, pharmacology
 talampanel: PD, pharmacology
 benserazide: PD, pharmacology
 RN (levodopa) 59-92-7; (6 quinoxalinecarboxylic acid piperidide) 154235-83-3; (talampanel) 161832-65-1, 161832-67-3; (benserazide)

14919-77-8, 322-35-0

CN (1) Cx 516; (2) Ly 300164

CO (1) Cortex (United States); (2) Lilly (United States); Research
Biochemicals

L113 ANSWER 2 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 96027659 EMBASE

DN 1996027659

TI Some central effects of GYKI 52466, a non-competitive **AMPA**
receptor antagonist.

AU Maj J.; Rogoz Z.; Skuza G.; Kolodziejczyk K.

CS Institute of Pharmacology, Polish Academy of Sciences, Smetna 12, 31-343
Krakow, Poland

SO Polish Journal of Pharmacology, (1995) 47/6 (501-507).

ISSN: 1230-6002 CODEN: PJPAE3

CY Poland

DT Journal; Article

FS 008 Neurology and Neurosurgery

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB GYKI 52466 [1-(4-aminophenyl)-4-methyl-7,8-methylenedioxy-5H-2,3-
benzodiazepine] has been described as a non-competitive **AMPA**
(non-NMDA glutamate) receptor antagonist. In the present paper some
behavioral effects of GYKI 52466 were studied in male Wistar rats and male
Albino Swiss mice. GYKI 52466 reduced the locomotor activity in normal
rats and mice, without evoking any symptoms of behavioral stimulation. The
CGP 37849-induced hyperlocomotion was increased by GYKI 52466. The
akinesia in monoamine-depleted rats was not affected by the drug studied.
The antiakinetik effect of L-DOPA was not changed by GYKI 52466, whereas
the antiakinetik effect of L-DOPA + CGP 37849 was decreased. GYKI 52466
increased the hyperlocomotion induced by apomorphine or cocaine. The drug
did not change the catalepsy induced by haloperidol or fluphenazine, as
well as the anticataleptic effect of CGP 37849. GYKI 52466 was inactive in
the forced swimming test, but increased the antidepressant effect of CGP
37849. The flexor and extensor muscle tone of the rats hind limb was not
modified by GYKI 52466. The results obtained indicate that GYKI 52466
shows a neuropharmacological profile similar but not identical with that
of the quinoxalines (competitive **AMPA** receptor antagonists)
studied previously.

CT Medical Descriptors:

*behavior

*central nervous system

akinesia

animal experiment

article

catalepsy

controlled study

drug antagonism

drug potentiation

extensor muscle

flexor muscle

forced swimming test

hyperactivity

intraperitoneal drug administration

locomotion

male

monoamine metabolism

mouse

muscle tone

nonhuman

rat

subcutaneous drug administration

Drug Descriptors:

*1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:

IT, drug interaction

*1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine:

PD, pharmacology

*quisqualic acid receptor: EC, endogenous compound

2 amino 4 methyl 5 phosphono 3 pentenoic acid: IT, drug interaction

2 amino 4 methyl 5 phosphono 3 pentenoic acid: CB, drug combination

2 amino 4 methyl 5 phosphono 3 pentenoic acid: PD, pharmacology

ampa receptor antagonist: PD, pharmacology

ampa receptor antagonist: IT, drug interaction

antidepressant agent: IT, drug interaction

antidepressant agent: PD, pharmacology

antidepressant agent: CB, drug combination

apomorphine: PD, pharmacology

apomorphine: IT, drug interaction

benserazide: PD, pharmacology

cocaine: IT, drug interaction

cocaine: PD, pharmacology

fluphenazine: PD, pharmacology

fluphenazine decanoate

glutamic acid antagonist: PD, pharmacology

glutamic acid antagonist: IT, drug interaction

haloperidol: PD, pharmacology

levodopa: IT, drug interaction

levodopa: PD, pharmacology

levodopa: CB, drug combination

metirosine: PD, pharmacology

quinoxaline derivative: PD, pharmacology

quinoxaline derivative: IT, drug interaction

reserpine: PD, pharmacology

RN (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine)
102771-26-6; (2 amino 4 methyl 5 phosphono 3 pentenoic acid) 127910-31-0;
(apomorphine) 314-19-2, 58-00-4; (benserazide) 14919-77-8,
322-35-0; (cocaine) 50-36-2, 53-21-4, 5937-29-1; (fluphenazine)
146-56-5, 69-23-8; (fluphenazine decanoate) 5002-47-1; (haloperidol)
52-86-8; (levodopa) **59-92-7**; (metirosine) 672-87-7; (reserpine)
50-55-5, 8001-95-4

CN (1) Ro 4 4602; (2) Cgp 37849; (3) Lyogen; (4) Rausedyl

CO (1) Hoffmann la roche (Switzerland); (2) Ciba geigy (Switzerland); (3) Byk
gulden (Germany); (4) Richter (Hungary); Sandoz (Switzerland); Merck
(Germany); Reanal (Hungary); Institute for drug research (Hungary); Sigma
(United States)

L113 ANSWER 3 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 95309948 EMBASE

DN 1995309948

TI Some behavioral effects of CNQX and NBQX, **AMPA** receptor
antagonists.

AU Maj J.; Rogoz Z.; Skuza G.; Jaros T.

CS Institute of Pharmacology, Polish Academy of Sciences, Smetna 12,31-343
Krakow, Poland

SO Polish Journal of Pharmacology, (1995) 47/4 (269-277).
ISSN: 1230-6002 CODEN: PJPAE3

CY Poland

DT Journal; Article

FS 008 Neurology and Neurosurgery

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB CNQX (6-cyano-7-nitroquinoxaline-2,3-dione) and NBQX (2,3-dihydroxy-6-
nitro-7-sulfamoyl-benzo[f]quinoxaline), two competitive **AMPA**
(non-NMDA glutamate) receptor antagonists, as well as their interaction
with CGP 37849, a competitive NMDA receptor antagonist, were studied in
rats and mice. CNQX and NBQX inhibited the locomotor activity of naive
rats. No symptoms of behavioral excitation were observed. CGP 37849
induced locomotor hyperactivity which was reduced by CNQX and NBQX. In

monoamine-depleted rats (pretreated with reserpine + .alpha.-methyl-p-tyrosine), none of the two quinoxalines nor CGP 37849 antagonized akinesia. The antiakinetik effect of L-DOPA was increased by CGP 37849, but not by CNQX or NBQX. The latter action of CGP 37849 was decreased by CNQX and NBQX. The antiakinetik effect of clonidine was not changed by CNQX. The locomotor hyperactivity induced by apomorphine or cocaine was not modified by CNQX. Neither of the quinoxalines changed the catalepsy induced by haloperidol or spiperone. The fluphenazine catalepsy was slightly decreased by CNQX and increased by NBQX. CNQX and NBQX were inactive in the forced swimming test; CNQX (but not NBQX) increased the CGP 37849-induced reduction of the immobility time. CNQX decreased the muscle tone of hind limbs in naive and monoamine-depleted rats. The obtained results indicate that the **AMPA** receptor antagonists differ in their neuropharmacological profile from CGP 37849, an NMDA receptor antagonist. There is no positive cooperation (except for the forced swimming test) between NMDA and **AMPA** receptor antagonists; on the contrary, an antagonistic interaction between them has been observed.

CT Medical Descriptors:

*behavior
akinesia
animal experiment
animal model
article
controlled study
drug antagonism
drug potentiation
forced swimming test
hyperactivity
intraperitoneal drug administration
locomotion
male
monoamine metabolism
mouse
muscle tone
nonhuman
rat
subcutaneous drug administration

Drug Descriptors:

*quisqualic acid receptor
*2 amino 4 methyl 5 phosphono 3 pentenoic acid: IT, drug interaction
*2 amino 4 methyl 5 phosphono 3 pentenoic acid: PD, pharmacology
 *6 cyano 7 nitro 2,3 quinoxalinedione: IT, drug interaction
 *6 cyano 7 nitro 2,3 quinoxalinedione: PD, pharmacology
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug interaction
*glutamic acid antagonist: PD, pharmacology
*glutamic acid antagonist: IT, drug interaction
*n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
*n methyl dextro aspartic acid receptor blocking agent: IT, drug interaction
 ampa receptor antagonist: PD, pharmacology
 ampa receptor antagonist: IT, drug interaction
apomorphine: PD, pharmacology
 benserazide: CB, drug combination
 benserazide: PD, pharmacology
clonidine: PD, pharmacology
cocaine: PD, pharmacology
fluphenazine: PD, pharmacology
fluphenazine: IT, drug interaction
fluphenazine decanoate
haloperidol: PD, pharmacology
 levodopa: CB, drug combination
 levodopa: IT, drug interaction

levodopa: PD, pharmacology
 metirosine: PD, pharmacology
 quinoxaline derivative: PD, pharmacology
 quinoxaline derivative: IT, drug interaction
 reserpine: PD, pharmacology
 spiperone: PD, pharmacology
 RN (2 amino 4 methyl 5 phosphono 3 pentenoic acid) 127910-31-0; (6 cyano 7
 nitro 2,3 quinoxalinedione) 115066-14-3; (6 nitro 7
 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (apomorphine)
 314-19-2, 58-00-4; (benserazide) 14919-77-8, 322-35-0;
 (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (cocaine) 50-36-2, 53-21-4,
 5937-29-1; (fluphenazine) 146-56-5, 69-23-8; (fluphenazine decanoate)
 5002-47-1; (haloperidol) 52-86-8; (levodopa) 59-92-7;
 (metirosine) 672-87-7; (reserpine) 50-55-5, 8001-95-4; (spiperone)
 749-02-0
 CN (1) Cgp 37849; (2) Lyogen; (3) Rausedyl; (4) Ro 4 4602
 CO (1) Ciba geigy (Switzerland); (2) Byk gulden (Germany); (3) Richter
 (Hungary); (4) Hoffmann la roche (Switzerland); Sandoz (Switzerland); Rbi
 (United States); Reanal (Hungary); Sigma (United States); Novo nordisk
 (Denmark)
 L113 ANSWER 4 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V..
 AN 95119361 EMBASE
 DN 1995119361
 TI Modulation of dopamine D1-mediated tuning behavior and striatal c-fos
 expression by the substantia nigra.
 AU Fenu S.; Carta A.; Morelli M.
 CS Department of Toxicology, Viale A. Diaz 182,09100 Cagliari, Italy
 SO Synapse, (1995) 19/4 (233-240).
 ISSN: 0887-4476 CODEN: SYNAET
 CY United States
 DT Journal; Article
 FS 008 Neurology and Neurosurgery
 030 Pharmacology
 037 Drug Literature Index
 052 Toxicology
 LA English
 SL English
 AB In order to study the possible contribution of the substantia nigra (SN)
 in the positive interaction between dopamine D1 receptor agonists and
 glutamate antagonists in unilaterally 6-hydroxydopamine (6-OHDA) lesioned
 rats, the effect of the D1 agonist, SKF 38393, was studied in combination
 with intranigral infusions of glutamate antagonists of the NMDA (MK 801,
 CPP) or AMPA (NBQX) type of receptor. Local infusion into the SN
 of the 6-OHDA lesioned side of MK 801, CPP or NBQX at doses inducing no or
 minimal behavioral effects significantly increased the turning behavior
 and the expression of c-fos induced, in the lesioned caudate-putamen
 (CPU), by a parenteral administration of SKF 38393. The same result was
 obtained after intra-SN infusion of the GABA agonist, muscimol. High doses
 of MK 801, CPP or muscimol infused into the SN produced intense
 contralateral turning per se and induced a sparse c-fos expression in the
 lesioned CPU which was antagonized by parenteral administration of MK 801.
 The results indicate that a depression of SN pars reticulata efferent
 neurons potentiates D1-mediated responses and suggest that this area may
 play a role in the positive interaction between glutamate antagonists and
 D1 receptor agonists.
 CT Medical Descriptors:
 *substantia nigra
 animal behavior
 animal experiment
 animal tissue
 article
 caudate nucleus
 controlled study
 drug infusion
 gene expression

immunohistochemistry
intracerebral drug administration
intravenous drug administration
male
neuropharmacology
nonhuman
oncogene c fos
priority journal
putamen
rat
Drug Descriptors:
*dopamine 1 receptor
n methyl dextro aspartic acid receptor
quisqualic acid receptor
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: CB, drug
combination
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: PD,
pharmacology
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: IT, drug
interaction
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: DO, drug dose
*2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine: CM, drug
comparison
*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CM, drug
comparison
*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug
interaction
*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD,
pharmacology
*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug
combination
*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose
*dizocilpine: DO, drug dose
*dizocilpine: IT, drug interaction
*dizocilpine: PD, pharmacology
*dizocilpine: CM, drug comparison
*dizocilpine: CB, drug combination
*dopamine 1 receptor blocking agent: DO, drug dose
*dopamine 1 receptor blocking agent: IT, drug interaction
*dopamine 1 receptor blocking agent: PD, pharmacology
*dopamine 1 receptor blocking agent: CM, drug comparison
*dopamine 1 receptor blocking agent: CB, drug combination
*glutamic acid antagonist: IT, drug interaction
*glutamic acid antagonist: DO, drug dose
*glutamic acid antagonist: CM, drug comparison
*glutamic acid antagonist: CB, drug combination
*glutamic acid antagonist: PD, pharmacology
4 aminobutyric acid receptor stimulating agent: CB, drug combination
4 aminobutyric acid receptor stimulating agent: PD, pharmacology
4 aminobutyric acid receptor stimulating agent: IT, drug interaction
4 aminobutyric acid receptor stimulating agent: DO, drug dose
4 aminobutyric acid receptor stimulating agent: CM, drug comparison
benserazide
desipramine
levodopa
muscimol: DO, drug dose
muscimol: PD, pharmacology
muscimol: IT, drug interaction
muscimol: CB, drug combination
muscimol: CM, drug comparison
n methyl dextro aspartic acid receptor blocking agent: CM, drug comparison
n methyl dextro aspartic acid receptor blocking agent: CB, drug
combination
n methyl dextro aspartic acid receptor blocking agent: IT, drug
interaction
n methyl dextro aspartic acid receptor blocking agent: DO, drug dose

n methyl dextro aspartic acid receptor blocking agent: PD, pharmacology
 oxidopamine: TO, drug toxicity
 RN (2,3,4,5 tetrahydro 7,8 dihydroxy 1 phenyl 1h 3 benzazepine) 67287-49-4;
 (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7;
 (dizocilpine) 77086-21-6; (benserazide) 14919-77-8, **322-35-0**;
 (desipramine) 50-47-5, 58-28-6; (levodopa) **59-92-7**; (muscimol)
 2763-96-4; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0
 CN (1) Skf 38393; (2) Mk 801
 CO (2) Rbi (United States); Hoffmann la roche (Switzerland); Ciba geigy
 (Switzerland); Sigma (Italy); Novo nordisk (Denmark)

L113 ANSWER 5 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 AN 94097346 EMBASE
 DN 1994097346
 TI Excitatory amino acid receptor antagonists modify regional cerebral
 metabolic responses to levodopa in 6-hydroxydopamine-lesioned rats.
 AU Engber T.M.; Anderson J.J.; Boldry R.C.; Papa S.M.; Kuo S.; Chase T.N.
 CS Experimental Therapeutics Branch, NINDS, Bethesda, MD 20892, United States
 SO Neuroscience, (1994) 59/2 (389-399).
 ISSN: 0306-4522 CODEN: NRSCDN
 CY United Kingdom
 DT Journal; Article
 FS 002 Physiology
 008 Neurology and Neurosurgery
 030 Pharmacology
 037 Drug Literature Index
 LA English
 SL English
 AB Excitatory amino acid receptor antagonists have been proposed as novel
 therapeutic agents to be used with levodopa in the treatment of
 Parkinson's disease. We examined the neural substrates for the interaction
 between levodopa and antagonists of either the .alpha.-amino-3-hydroxy-5-
 methylisoxazole- 4-propionic acid or N-methyl-D-aspartate type of
 excitatory amino acid receptor using 2-deoxyglucose autoradiography. Thus,
 we compared the effects of the .alpha.-amino-3-hydroxy-5-methylisoxazole-4-
 propionic acid receptor antagonist 2,3-dihydroxy-6-nitro-7-sulfamoyl-
 benzo(F)quinoxaline (10 mg/kg, i.v.) and the N-methyl-D-aspartate
 antagonist MK-801 (0.1 mg/kg, i.v.) on cerebral metabolic responses to
 levodopa (25 mg/kg, i.v. with 12.5 mg/kg benserazide) in rats with a
 unilateral nigrostriatal pathway lesion. Levodopa increased glucose
 utilization ipsilateral to the lesion in substantia nigra pars reticula
 (up to 104%), entopeduncular nucleus (up 90%) and subthalamic nucleus (up
 30%), indicating that levodopa alters striatal output through the
 striatonigral, striatoentopeduncular and striatopallidal pathways.
 Levodopa also decreased metabolic rate in lateral habenula (down 39%), a
 target of projections from entopeduncular nucleus, implying a reduction in
 basal ganglia output. 2,3-Dihydroxy-6-nitro-7-sulfamoyl-
 benzo(F)quinoxaline and MK- 801 by themselves did not affect glucose
 utilization in any of these regions. Pretreatment with
 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo(F)quinoxaline reduced the effect
 of levodopa in substantia nigra pars reticulata but not in entopeduncular
 nucleus or subthalamic nucleus, while MK-801 attenuated the effect of
 levodopa in all three of these structures; neither 2,3-dihydroxy-
 6-nitro-7-sulfamoyl-benzo(F)quinoxaline nor MK-801 altered the effect of
 levodopa in lateral habenula. When given at the same doses to a separate
 group of lesioned animals, neither 2,3-dihydroxy-6-nitro-7-sulfamoyl-
 benzo(F)quinoxaline nor MK-801 affected rotational behavior elicited by
 levodopa. These findings indicate that .alpha.-amino-3-hydroxy-5-
 methylisoxazole- 4-propionic acid and N-methyl-D-aspartate receptor
 antagonists differentially modify dopamine receptor-mediated striatal
 output. .alpha.-Amino-3-hydroxy-5- methylisoxazole-4-propionic acid
 receptor blockade may preferentially attenuate the effect of dopamine
 receptor activation on the striatonigral pathway, while
 N-methyl-D-aspartate blockade appears to reduce the actions of dopamine on
 the striatonigral, striatoentopeduncular and striatopallidal pathways.
 However, the lack of effect of both 2,3-dihydroxy-6-nitro-7-

sulfamoyl-benzo(F)quinoxaline and MK-801 on levodopa-induced rotational behavior and reduced metabolic rate in the lateral habenula suggests that neither .alpha.-amino-3-hydroxy-5-methylisoxazole-4-propionic acid nor N-methyl- D-aspartate receptor blockade diminishes the net effect of levodopa on basal ganglia output.

- CT Medical Descriptors:
 *nigrostriatal system
 animal experiment
 animal model
 animal tissue
 article
 autoradiography
 brain region
 circling behavior
 controlled study
 intravenous drug administration
 male
 nonhuman
 parkinson disease: DT, drug therapy
 priority journal
 rat
 Drug Descriptors:
 *dopamine receptor
 *glutamate receptor
 *n methyl dextro aspartic acid receptor
 quisqualic acid receptor
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CM, drug comparison
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: IT, drug interaction
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology
 *deoxyglucose
 *dizocilpine: CB, drug combination
 *dizocilpine: CM, drug comparison
 *dizocilpine: IT, drug interaction
 *dizocilpine: PD, pharmacology
 *glutamic acid antagonist: PD, pharmacology
 *glutamic acid antagonist: CB, drug combination
 *glutamic acid antagonist: CM, drug comparison
 *glutamic acid antagonist: IT, drug interaction
 *levodopa: IT, drug interaction
 *levodopa: PD, pharmacology
 *oxidopamine: TO, drug toxicity
 benserazide: CB, drug combination
- RN (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7;
 (deoxyglucose) 154-17-6; (dizocilpine) 77086-21-6; (levodopa) 59-92-7; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0; (benserazide) 14919-77-8, 322-35-0
- CN (1) Mk 801
- CO (1) Rbi (United States); Sigma (United States); Novo nordisk (Denmark); Hoffmann la roche (United States)
- L113 ANSWER 6 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 AN 94039675 EMBASE
 DN 1994039675
 TI The AMPA antagonists NBQX and GYKI 52466 do not counteract neuroleptic- induced catalepsy.
 AU Zadow B.; Schmidt W.J.
 CS Neuropharmacology Division, Zoological Institute, University of Tübingen, Mohlstrasse 54/1, D-72074 Tübingen, Germany
 SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1994) 349/1 (61-65). ISSN: 0028-1298 CODEN: NSAPCC
 CY Germany

DT Journal; Article
 FS 008 Neurology and Neurosurgery
 030 Pharmacology
 037 Drug Literature Index
 LA English
 SL English
 AB The **AMPA** antagonists NBQX (2.5, 5, 10 mg/kg) and GYKI 52466 (4.8, 8 mg/kg) were investigated in haloperidol (0.5 mg/kg)-induced catalepsy in the rat. The effects of **AMPA** antagonists administered either alone or in combination with the noncompetitive NMDA antagonist dizocilpine (0.02 mg/kg), with the dopamine D-2 agonist quinpirole (1 mg/kg) or with L-DOPA (50, 100 mg/kg plus benserazide) were tested. NBQX or GYKI 52466 did not exert anticataleptic effects, neither alone nor in combination with dizocilpine, quinpirole or L- DOPA. Thus, in the rat inhibition of **AMPA** receptors with NBQX or GYKI 52466 does not have effects predictive for an antiparkinsonian potential.

CT Medical Descriptors:
 *catalepsy
 animal experiment
 article
 controlled study
 intraperitoneal drug administration
 male
 nonhuman
 oral drug administration
 rat
 Drug Descriptors:
 *excitatory amino acid receptor
 quisqualic acid receptor
 *1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine: PD, pharmacology
 *1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine: DO, drug dose
 *1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine: CB, drug combination
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination
 *6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology
 *amino acid receptor blocking agent: CB, drug combination
 *amino acid receptor blocking agent: DO, drug dose
 *amino acid receptor blocking agent: PD, pharmacology
 *benserazide: CB, drug combination
 *neuroleptic agent: PD, pharmacology
 ampa receptor antagonist: CB, drug combination
 ampa receptor antagonist: DO, drug dose
 ampa receptor antagonist: PD, pharmacology
 benserazide plus levodopa: PD, pharmacology
 benserazide plus levodopa: CB, drug combination
 dizocilpine: PD, pharmacology
 dizocilpine: CB, drug combination
 dopamine 2 receptor stimulating agent: CB, drug combination
 dopamine 2 receptor stimulating agent: PD, pharmacology
 levodopa: CB, drug combination
 quinpirole: CB, drug combination
 quinpirole: PD, pharmacology

RN (1 (4 aminophenyl) 4 methyl 7,8 methylenedioxy 5h 2,3 benzodiazepine) 102771-26-6; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (benserazide) 14919-77-8, 322-35-0; (benserazide plus levodopa) 37270-69-2; (dizocilpine) 77086-21-6; (levodopa) 59-92-7; (quinpirole) 73625-62-4, 80373-22-4, 85760-75-4, 85798-08-9

CN (1) Mk 801; (2) Madopar; (3) Gyki 52466
 CO (1) Merck sharp and dohme (Germany); (2) Hoffmann la roche (Germany); (3) Institute for drug research (Hungary); Novo nordisk (Denmark); Janssen

(Germany); Biotrend (Germany)

L113 ANSWER 7 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 AN 93131307 EMBASE
 DN 1993131307
 TI Glutamate-dopamine interactions in the basal ganglia: Relationship to Parkinson's disease.
 AU Greenamyre J.T.
 CS Department of Neurology, University of Rochester, 601 Elmwood Ave, Rochester, NY 14642, United States
 SO Journal of Neural Transmission - General Section, (1993) 91/2-3 (255-269). ISSN: 0300-9564 CODEN: JNTMAH
 CY Austria
 DT Journal; General Review
 FS 008 Neurology and Neurosurgery
 030 Pharmacology
 037 Drug Literature Index
 038 Adverse Reactions Titles
 LA English
 SL English
 AB Current antiparkinsonian therapies focus on either replacing dopamine via precursor (L-DOPA) administration, or directly stimulating postsynaptic dopamine receptors with dopamine agonists. Unfortunately, this approach is associated with numerous side effects and these drugs lose efficacy with disease progression. This article reviews recent evidence which suggests that negative modulation of glutamatergic neurotransmission has antiparkinsonian effects in a variety of rodent and primate models of parkinsonism. The pronounced synergism between dopaminergic agents and glutamate receptor antagonists may provide a means of using very low doses of the two drug classes in concert to treat Parkinson's disease effectively and minimize dose-related drug side effects.
 CT Medical Descriptors:
 *basal ganglion
 *parkinson disease: ET, etiology
 *parkinson disease: DT, drug therapy
 animal model
 disease course
 drug effect
 drug efficacy
 drug potentiation
 functional anatomy
 modulation
 neuroanatomy
 neurotransmission
 nonhuman
 primate
 priority journal
 review
 rodent
 side effect
 subthalamic nucleus
 Drug Descriptors:
 dopamine receptor
 n methyl dextro aspartic acid receptor
 *dopamine: EC, endogenous compound
 *glutamic acid: EC, endogenous compound
 1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: PD, pharmacology
 1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: DT, drug therapy
 6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD, pharmacology
 6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DT, drug therapy
 6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug combination
 carbidopa: PD, pharmacology
 carbidopa: CB, drug combination
 dopamine receptor stimulating agent: DT, drug therapy
 dopamine receptor stimulating agent: IT, drug interaction

dopamine receptor stimulating agent: DO, drug dose
dopamine receptor stimulating agent: CB, drug combination
dopamine receptor stimulating agent: AE, adverse drug reaction
glutamic acid antagonist: CB, drug combination
glutamic acid antagonist: DO, drug dose
glutamic acid antagonist: IT, drug interaction
glutamic acid antagonist: DT, drug therapy

levodopa: PD, pharmacology

levodopa: DT, drug therapy

levodopa: CB, drug combination

levodopa: AE, adverse drug reaction

RN (dopamine) 51-61-6, 62-31-7; (glutamic acid) 11070-68-1, 138-15-8, 56-86-0, 6899-05-4; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (carbidopa) 28860-95-9; (levodopa) 59-92-7

L113 ANSWER 8 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 93058820 EMBASE

DN 1993058820

TI Excitatory amino acid antagonists and Parkinson's disease.

AU Rosario Luquin M.; Martinez-Lage J.M.

CS Department Neurology/Neurosurgery, Clinica Universitaria, Medical School, Pamplona, Spain

SO New Trends in Clinical Neuropharmacology, (1992) 6/1-4 (43-47).

ISSN: 0393-5345 CODEN: NTCNEP

CY Italy

DT Journal; Article

FS 008 Neurology and Neurosurgery

052 Toxicology

030 Pharmacology

037 Drug Literature Index

LA English

SL English

AB We have studied the motor response induced by the administration of the AMPA-antagonist NBQX given alone or simultaneously with l-dopa to 2 parkinsonian monkeys. NBQX (1, 2 and 4 mg/kg im) failed to reverse parkinsonism. Similarly, co-administration of NBQX (1 mg/kg) plus l-dopa (12.5, 25 and 50 mg orally) did not modify the motor improvement and dyskinesia induced by l-dopa. These results suggest that NBQX can not be considered as a useful treatment for Parkinson's disease.

CT Medical Descriptors:

*motor dysfunction

*parkinson disease: DT, drug therapy

animal experiment

animal model

article

controlled study

dyskinesia

intramuscular drug administration

monkey

nonhuman

oral drug administration

Drug Descriptors:

*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DO, drug dose

*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: CB, drug

combination

*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: DT, drug

therapy

*6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione: PD,

pharmacology

*amino acid receptor blocking agent: PD, pharmacology

*amino acid receptor blocking agent: DT, drug therapy

*amino acid receptor blocking agent: DO, drug dose

*amino acid receptor blocking agent: CB, drug combination

*levodopa: CB, drug combination

*levodopa: DT, drug therapy

*levodopa: PD, pharmacology
 *levodopa: TO, drug toxicity
 *levodopa: DO, drug dose
 1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine: TO, drug toxicity
 benserazide: DT, drug therapy
 benserazide: CB, drug combination
 benserazide plus levodopa
 naxagolide: DT, drug therapy
 RN (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione) 118876-58-7; (levodopa) 59-92-7; (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (benserazide) 14919-77-8, 322-35-0; (benserazide plus levodopa) 37270-69-2; (naxagolide) 88058-88-2
 CN (1) Madopar
 CO (1) Hoffmann la roche; Novo nordisk
 L113 ANSWER 9 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
 AN 91340439 EMBASE
 DN 1991340439
 TI The **AMPA** receptor antagonist NBQX has antiparkinsonian effects in monoamine-depleted rats and MPTP-treated monkeys.
 AU Klockgether T.; Turski L.; Honore T.; Zhang Z.; Gash D.M.; Kurlan R.; Greenamyre J.T.
 CS Department of Neurology, Rochester Univ. Medical Center, Box 673, 601 Elmwood Ave, Rochester, NY 14642, United States
 SO Annals of Neurology, (1991) 30/5 (717-723).
 ISSN: 0364-5134 CODEN: ANNE3
 CY United States
 DT Journal; Article
 FS 008 Neurology and Neurosurgery
 030 Pharmacology
 037 Drug Literature Index
 LA English
 SL English
 AB Abnormally increased subthalamic nucleus output to the internal pallidal segment and the reticular part of the substantia nigra plays a critical pathophysiological role in the development of parkinsonism. Because synaptic transmission of subthalamic output is glutamatergic and mediated, in part, by the .alpha.-amino-3-hydroxy-5-methyl-4-isoxazole propionate (**AMPA**) subtype of glutamate receptor, **AMPA** receptor antagonists may possess antiparkinsonian properties. We report that in monoamine-depleted rats, 2,3-dihydroxy-6-nitro-7-sulfamoylbenzo(f)quinoxaline (NBQX) (Novo-Nordisk, Copenhagen, Denmark)-a selective antagonist of the **AMPA** subtype of glutamate receptor-suppressed muscular rigidity but had no effect on akinesia. NBQX microinjected into the subthalamic nucleus, internal pallidal segment, and reticular part of the substantia nigra, but not into the laterodorsal neostriatum of the rats, stimulated locomotor activity and reduced muscular rigidity. In aged Rhesus monkeys with bilateral 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced parkinsonism, intramuscular NBQX produced clinically apparent improvement in akinesia, tremor, posture, and gross motor skills. NBQX also potentiated the antiparkinsonian effects of L-3,4-dihydroxyphenylalanine in both rats and monkeys. Blockade of excitatory synaptic transmission by **AMPA** receptor antagonists may provide a new therapeutic strategy for Parkinson's disease (PD).
 CT Medical Descriptors:
 *parkinsonism
 *rigidity
 animal model
 article
 female
 intramuscular drug administration
 male
 monkey
 nonhuman
 priority journal
 Drug Descriptors:

*1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine
 *reserpine
 6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione
carbidopa plus levodopa

RN (1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine) 28289-54-5; (reserpine)
 50-55-5, 8001-95-4; (6 nitro 7 sulfamoylbenzo[f]quinoxaline 2,3 dione)
 118876-58-7; (carbidopa plus levodopa) **57308-51-7**

CN **(1) Sinemet**

CO (1) Merck sharp and dohme; Novo nordisk (Denmark)

L113 ANSWER 10 OF 10 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

AN 80251895 EMBASE

DN 1980251895

TI Kainic acid-induced wet dog shakes in rats. The relation to central neurotransmitters.

AU Kleinrok Z.; Turski L.

CS Dept. Pharmacol., Inst. Clin. Pathol., Med. Sch., PL-20-090 Lublin, Poland

SO Naunyn-Schmiedeberg's Archives of Pharmacology, (1980) 314/1 (37-46).

CODEN: NSAPCC

CY Germany

DT Journal

FS 030 Pharmacology

050 Epilepsy

037 Drug Literature Index

008 Neurology and Neurosurgery

LA English

AB Following the intracerebroventricular administration of kainic acid (KA), rats showed wet dog shakes (WDS) in a dose-dependent manner. DL-.alpha.-amino adipic acid and L-glutamic acid diethylester blocked WDS behavior induced by 0.05 .mu.g of KA. Noradrenaline, clonidine, yohimbine and apomorphine also significantly blocked KA-induced WDS. Phentolamine and propranolol did not affect WDS. FLA 63, 6-OHDA lesion and bilateralis electrolytic lesion to locus coeruleus markedly enhanced, but L-Dopa blocked WDS behavior. Moreover, the KA-induced shaking behavior was blocked by .alpha.-methyl-p-tyrosine and haloperidol. Cyproheptadine and methergoline also blocked WDS. p-Chlorophenylalanine, 5,6-DHT lesion, electrolytic lesions to dorsal and medial raphe nuclei showed no effect on WDS behavior, but L-5-hydroxytryptophan efficiently blocked it. Atropine and morphine considerably blocked KA-induced WDS behavior, but pilocarpine and nalorphine showed no effect. Bicuculline significantly enhanced, but aminoxyacetic acid blocked WDS. Intracerebroventricularly administered KA dose-dependently decreased the concentrations of noradrenaline and dopamine in the whole rat brain. The brain concentration of 5-hydroxytryptamine was unchanged. In contrast the concentration of 5-hydroxyindoleacetic acid increased. KA was ineffective regarding the GABA concentration and GAD activity. KA dose-dependently accelerated the disappearance of brain noradrenaline and dopamine after inhibition of catecholamine synthesis. KA, following inhibition of monoamine oxidase, increased the accumulation of 5-hydroxytryptamine, but failed to change the rate of decline of 5-hydroxyindoleacetic acid. KA failed to change the disappearance of brain 5-hydroxytryptamine after inhibition of its synthesis by PCPA. It is suggested that KA-induced WDS behavior is independent from the increased activity of serotonergic neurons in the central nervous system. KA-induced WDS appears to be under the inhibitory control of noradrenergic and GABA-ergic activity. The weaker inhibitory effect upon this behavior showed also dopaminergic and serotonergic neurons. The present experiments showed the close relationship between KA-induced WDS and shaking behavior in morphine abstinence, but basic differences in WDS behavior caused by excessive stimulation of serotonergic receptors.

CT Medical Descriptors:

*5,6 dihydroxytryptophan

*brain injury

*locus ceruleus

*raphe nucleus

*wet dog shakes

withdrawal syndrome
 intracerebral drug administration
 dose response
 drug comparison
 drug withdrawal
 rat
 drug response
 therapy
 central nervous system
 animal experiment
 intracerebroventricular drug administration
 intraperitoneal drug administration
 subcutaneous drug administration
 Drug Descriptors:
 *4 aminobutyric acid
 *5 hydroxytryptophan
 *oxidopamine
 *aminoadipic acid
 *apomorphine
 *atropine
 *benserazide
 *bis(4 methyl 1 homopiperazinylthiocarbonyl)disulfide
 *aminooxyacetic acid
 *clonidine
 *cyproheptadine
 *dopamine
 *fencloine
 *glutamic acid diethyl ester
 *haloperidol
 *kainic acid
 *levodopa
 *metergoline
 *metirosine
 *morphine
 *nalorphine
 *neurotransmitter
 *noradrenalin
 *phentolamine
 *pilocarpine
 *serotonin
 *yohimbine
 bicuculline
 propranolol

RN (4 aminobutyric acid) 28805-76-7, 56-12-2; (5 hydroxytryptophan)
 4350-09-8, 56-69-9; (oxidopamine) 1199-18-4, 28094-15-7, 636-00-0;
 (aminoadipic acid) 52047-41-3; (apomorphine) 314-19-2, 58-00-4; (atropine)
 51-55-8, 55-48-1; (benserazide) 14919-77-8, 322-35-0; (bis(4
 methyl 1 homopiperazinylthiocarbonyl)disulfide) 26087-98-9;
 (aminooxyacetic acid) 2921-14-4, 645-88-5; (clonidine) 4205-90-7,
 4205-91-8, 57066-25-8; (cyproheptadine) 129-03-3, 969-33-5; (dopamine)
 51-61-6, 62-31-7; (fencloine) 1991-78-2, 7424-00-2; (glutamic acid
 diethyl ester) 16450-41-2; (haloperidol) 52-86-8; (kainic acid) 487-79-6;
 (levodopa) 59-92-7; (metergoline) 17692-51-2; (metirosine)
 672-87-7; (morphine) 52-26-6, 57-27-2; (nalorphine) 1041-90-3, 57-29-4,
 62-67-9; (noradrenalin) 1407-84-7, 51-41-2; (phentolamine) 50-60-2,
 73-05-2; (pilocarpine) 148-72-1, 54-71-7, 92-13-7; (serotonin) 50-67-9;
 (yohimbine) 146-48-5, 65-19-0; (bicuculline) 485-49-4; (propranolol)
 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6

CN Fla 63; Ro 4 4602

CO Sigma (United States); Polfa (Poland); Sandoz (Luxembourg); Merck
 (Germany); Vacom (Yugoslavia); Koch light (United Kingdom); Ciba geigy
 (Switzerland); Chinoin (Hungary); Kistner (Sweden); Boehringer ingelheim
 (Germany); Richter (Hungary); Roche (Switzerland)

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L128 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS

AN 2001:147868 BIOSIS

DN PREV200100147868

TI Atropisomeric **quinazolin-4-one** derivatives are potent
noncompetitive **alpha-amino-3-hydroxy-5-methyl**
-4-isoxazolepropionic acid (AMPA) receptor
antagonists.

AU **Welch, W. M.**; Ewing, F. E.; Huang, J.; **Menniti, F. S.**;
Pagnozzi, M. J.; Kelly, K.; Seymour, P. A.; Guanowsky, V.; Guhan, S.;
Guinn, M. R.; Critchett, D.; Lazzaro, J.; Ganong, A. H.; DeVries, K. M.;
Staigers, T. L.; **Chenard, B. L.** (1)

CS (1) Global Research and Development, Groton Laboratories, Pfizer Inc.,
Groton, CT, 06340: chenardbl@groton.pfizer.com USA

SO Bioorganic & Medicinal Chemistry Letters, (22 January, 2001) Vol. 11, No.
2, pp: 177-181. print.
ISSN: 0960-894X.

DT Article

LA English

SL English

AB Piriqualone (1) was found to be an antagonist of **AMPA** receptors.
Structure-activity optimization was conducted on each of the three rings
in 1 to afford a series of potent and selective antagonists. The
sterically crowded environment surrounding the N-3 aryl group provided
sufficient thermal stability for atropisomers to be isolated. Separation
of these atropisomers resulted in the identification of (+)-38
(CP-465,022), a compound that binds to the **AMPA** receptor with
high affinity (IC50=36nM) and displays potent anticonvulsant activity.

CC Pharmacology - Neuropharmacology *22024

Biochemical Studies - General *10060

Pathology, General and Miscellaneous - Therapy *12512

Pharmacology - General *22002

IT Major Concepts

Biochemistry and Molecular Biophysics; Pharmaceuticals (Pharmacology)

IT Chemicals & Biochemicals

CP-465,022: anticonvulsant - drug; **alpha-amino-3-**
hydroxy-5-methyl-4-isoxazolepropionic acid
receptor; piriqualone: **alpha-amino-3-hydroxy-5-**
methyl-4-isoxazolepropionic acid receptor antagonist;
quinazolin-4-one: **alpha-amino-3-hydroxy-5-**
methyl-4-isoxazolepropionic acid receptor antagonist,
derivatives

RN 199655-36-2 (CP-465,022)

1897-89-8 (PIRIQUALONE)

491-36-1 (**QUINAZOLIN-4-ONE**)

L128 ANSWER 2 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS

AN 2001:45788 BIOSIS

DN PREV200100045788

TI **Quinazoline-4-one** **AMPA** antagonists.

AU **Chenard, Bertrand L.**; **Welch, Willard M.** (1)

CS (1) Mystic, CT USA

ASSIGNEE: Pfizer Inc

PI US 6060479 May 09, 2000
SO Official Gazette of the United States Patent and Trademark Office Patents,
(May 9, 2000) Vol. 1234, No. 2, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB The present invention relates to novel **quinazolin-4-one**
derivatives of the formula I, as defined in the specification,
pharmaceutical compositions containing such compounds the use of such
compounds to treat neurodegenerative, psychotropic, and drug and alcohol
induced central and peripheral nervous system disorders.
NCL 514258000
IT Major Concepts
Neurology (Human Medicine, Medical Sciences); Psychiatry (Human
Medicine, Medical Sciences); Pharmaceuticals (Pharmacology)
IT Diseases
nervous system disorders: alcohol-induced, drug-induced, nervous system
disease; neurodegenerative disorders: nervous system disease;
psychotropic disorder: behavioral and mental disorders, nervous system
disease
IT Chemicals & Biochemicals
quinazolin-4-one: AMPA antagonist, derivatives,
pharmaceutical
RN 491-36-1 (**QUINAZOLIN-4-ONE**)

L128 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:355669 BIOSIS
DN PREV200000355669
TI Methaqualone derivatives are potent noncompetitive **AMPA** receptor
antagonists.
AU **Chenard, B. L. (1); Menniti, F. S.; Pagnozzi, M. J.;**
Shenk, K. D.; Ewing, F. E.; Welch, W. M.
CS (1) Central Research Division, Pfizer Inc., Groton, CT, 06340 USA
SO Bioorganic & Medicinal Chemistry Letters, (5 June, 2000) Vol. 10, No. 11,
pp. 1203-1205. print.
ISSN: 0960-894X.
DT Article
LA English
SL English
AB **Quinazolin-4-one** derivatives of methaqualone substituted at C-2
define a new class of noncompetitive antagonists at **AMPA**
receptors.
CC Biochemical Studies - General *10060
Pathology, General and Miscellaneous - Therapy *12512
Nervous System - Physiology and Biochemistry *20504
Pharmacology - General *22002
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural
Coordination); Pharmacology
IT Parts, Structures, & Systems of Organisms
central nervous system: nervous system
IT Chemicals & Biochemicals
2-amino-3-(3-hydroxy-5-methyl-4-
isoxazolyl)-propionate receptor; methaqualone
derivative: anticonvulsant activity, noncompetitive 2-amino
-3-(3-hydroxy-5-methyl-4-**isoxazolyl)-**
propionate receptor antagonist, pyridine ring modification;
quinazolin-4-one: synthesis
RN 491-36-1 (**QUINAZOLIN-4-ONE**)

L128 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:222771 BIOSIS
DN PREV200000222771
TI Discovery of a potent and selective series of noncompetitive
quinazolinone AMPA antagonists.
AU **Welch, Willard M. (1); Huang, J. H. (1); Ewing, F. E. (1);**

Menniti, F. S. (1); Pagnozzi, M. J. (1); Banker, M. J. (1);
Devries, K. M. (1)
CS (1) Department of Medicinal Chemistry, Pfizer Inc, Eastern Point Road,
Groton, CT, 06340 USA
~~SC~~ Abstracts of Papers American Chemical Society, (2000) Vol. 219, No. 1-2,
pp. MEDI 325.
Meeting Info.: 219th Meeting of the American Chemical Society. San
Francisco, California, USA March 26-30, 2000 American Chemical Society
. ISSN: 0065-7727.
DT Conference
LA English
SL English
CC Pharmacology - General *22002
Cytology and Cytochemistry - General *02502
Biochemical Methods - General *10050
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Pathology, General and Miscellaneous - Therapy *12512
Metabolism - General Metabolism; Metabolic Pathways *13002
Pathology, General and Miscellaneous - General *12502
Biochemical Studies - General *10060
General Biology - Symposia, Transactions and Proceedings of Conferences,
Congresses, Review Annuals *00520
IT Major Concepts
Pharmacology
IT Chemicals & Biochemicals
AMPA receptors [alpha-amino-3-hydroxy-5-
methyl-isoxazole propionate receptors];
noncompetitive quinazolinone AMPA receptor
antagonists: molecular properties, pharmaceuticals, pharmacodynamics,
pharmacological properties, synthesis
IT Miscellaneous Descriptors
drug discovery; structure-activity relationships; Meeting Abstract

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L9 ANSWER 1 OF 4 CAPLUS COPYRIGHT 1999 ACS

PY 1999

1999

1999

1999

AN 1999:175749 CAPLUS

DN 130:218317

TI AMPA antagonists for the treatment of dyskinesias associated with dopamine agonist therapy

IN Chenard, Bertrand Leo; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.

PA Pfizer Products Inc., USA

SO Eur. Pat. Appl., 22 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K031-505

ICI A61K031-505, A61K031-195, A61K031-15

CC 1-11 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 900568	A2	19990310	EP 1998-307181	19980904
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 11158072	A2	19990615	JP 1998-245269	19980831
	AU 9883120	A1	19990318	AU 1998-83120	19980904
	CA 2246839	AA	19990305	CA 1998-2246839	19980908
PRAI	US 1997-58098		19970905		

OS MARPAT 130:218317

AB The invention relates to a method of treating dyskinesias assocd. with dopamine agonist therapy in a mammal which comprises administering to said mammal a compd., as defined herein, which is an antagonist of the AMPA receptor. Dopamine agonist therapy, as referred to in the present invention, is generally used in the treatment of a central nervous system disorder such as Parkinson's disease. One example compd. of the 212 claimed was (S)-3-(2-chlorophenyl)-2-[2-(5-diethylaminomethyl-2-fluorophenyl)vinyl]-6-fluoro-3H-quinazolin-4-one.

ST AMPA antagonist dyskinesia dopamine agonist

IT Drug delivery systems

Parkinson's disease

(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT AMPA receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT Dyskinesia (nervous system)

(Parkinson's-assocd.; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 51-61-6, Dopamine, biological studies 59-92-7, biological studies
322-35-0, Benserazide 3257-47-4 28860-95-9, Carbidopa 199655-53-3
199655-54-4 199655-56-6 199655-57-7 199655-58-8 199655-59-9
199655-61-3 199655-62-4 199655-63-5 199655-64-6 199655-65-7
199655-66-8 199655-67-9 199655-68-0 199655-69-1 199655-70-4
199655-71-5 199655-72-6 199655-75-9 199655-76-0 199655-77-1
199655-78-2 199655-80-6 199655-81-7 199655-82-8

199655-84-0	199655-86-2	199655-87-3	199655-88-4	199655-89-5
199655-90-8	199655-91-9	199656-00-3	199656-44-5	212710-60-6
212710-61-7	212710-62-8	212710-64-0	212710-65-1	212710-66-2
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212850-74-3	212850-78-7	212850-79-8	212850-80-1	212850-81-2
212850-82-3	212916-59-1	212916-65-9	217821-32-4	217821-33-5
217821-34-6	217821-35-7	217821-36-8	217821-37-9	217821-38-0
217821-39-1	217821-41-5	217821-42-6	217942-51-3	217942-54-6
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221152-18-7	221152-21-2	221152-23-4	221152-26-7	221152-29-0
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221167-95-9	221167-96-0	221167-97-1	221167-99-3	221168-01-0
221168-06-5	221168-10-1	221168-22-5	221168-25-8	221168-27-0
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221177-88-4	221177-89-5	221177-90-8	221177-91-9	

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 77521-29-0, Ampa

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (antagonists; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 9042-64-2, Dopa decarboxylase

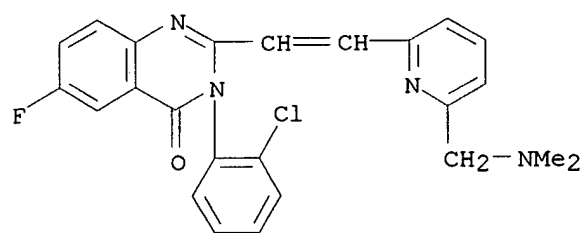
RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 199655-81-7

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (AMPA antagonists for treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d py all hitstr 2

L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 1999 ACS

PY 1999

1999

1999

1999

AN 1999:175748 CAPLUS

DN 130:209717

TI Preparation of 3-(2-chlorophenyl)-2-[2-(6-diethylaminomethylpyridin-2-yl)vinyl]-6-fluoro-3H-quinazolin-4-one as an AMPA antagonist for the treatment of dyskinesias associated with dopamine agonist therapy.

IN Chenard, Bertrand Leo; Greenamyre, John Timothy; Menniti, Frank Samuel; Welch, Willard McKowan, Jr.

PA Pfizer Products Inc., USA

SO Eur. Pat. Appl., 6 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM A61K031-505

ICI A61K031-505, A61K031-195, A61K031-15

CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 900567	A2	19990310	EP 1998-306661	19980820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2246560	AA	19990305	CA 1998-2246560	19980903
	JP 11139991	A2	19990525	JP 1998-249644	19980903
	AU 9883193	A1	19990318	AU 1998-83193	19980907
PRAI	US 1997-57965		19970905		
AB	A method for the treatment of dyskinesias assocd. with dopamine agonist therapy comprising administration of an AMPA antagonist is claimed (no data). Thus, 3-(2-chlorophenyl)-6-fluoro-2-methyl-4-(3H)-quinazolinone (prepn. given) was refluxed with 2,6-pyridinedicarboxaldehyde, ZnCl ₂ , and Ac ₂ O in dioxane to give 33% 6-[2-[3-(2-chlorophenyl)-6-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl]vinyl]pyridine-2-carboxaldehyde. This was stirred with Et ₂ NH and NaBH(AcO) ₃ in CH ₂ Cl ₂ to give 24% title compd. as the monomaleate salt.				
ST	chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone prepn AMPA antagonist; quinazolinone chlorophenyldiethylaminomethylpyridinylvinyl prepn AMPA antagonist; dyskinesia treatment AMPA antagonist chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone				
IT	AMPA receptors				
	RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)				
	(antagonists; prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)				
IT	Dyskinesia (nervous system)				
	(treatment; prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)				
IT	220931-86-2P				
	RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
	(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-				

one as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **199655-81-7**
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 59-92-7, L-Dopa, miscellaneous 322-35-0, Benserazide 28860-95-9, Carbidopa
 RL: MSC (Miscellaneous)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT 95-51-2, 2-Chloroaniline 109-89-7, reactions 320-98-9 5431-44-7, 2,6-Pyridinedicarboxaldehyde
 RL: RCT (Reactant)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

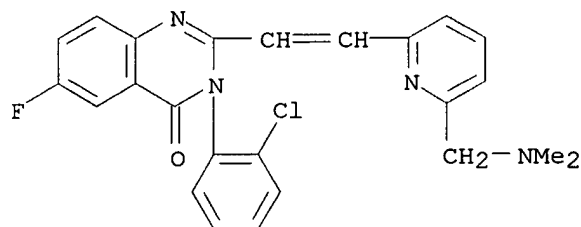
IT 38520-78-4P 49579-12-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

IT **220931-86-2P**
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolinone as an AMPA antagonist for the treatment of dyskinesias assocd. with dopamine agonist therapy)

RN 220931-86-2 CAPLUS
 CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

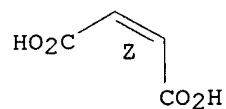
CRN 199655-81-7
 CMF C24 H20 Cl F N4 O



CM 2

CRN 110-16-7
 CMF C4 H4 O4
 CDES 2:Z

Double bond geometry as shown.



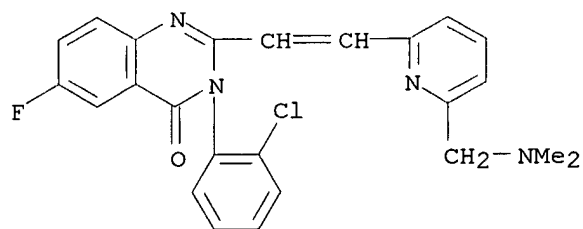
IT 199655-81-7

RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of chlorophenyldiethylaminomethylpyridinylvinylfluoroquinazolin-
one as an AMPA antagonist for the treatment of dyskinesias assocd. with
dopamine agonist therapy)

RN 199655-81-7 CAPLUS

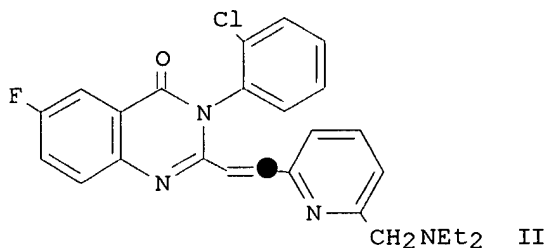
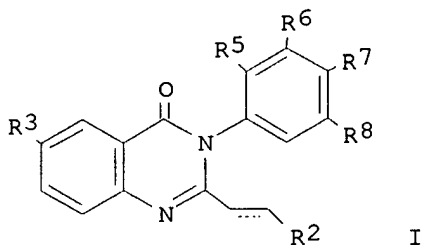
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-
pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d py all hitstr 3

L9 ANSWER 3 OF 4 CAPLUS COPYRIGHT 1999 ACS
PY 1998
1998
AN 1998:608605 CAPLUS
DN 129:230733
TI Preparation of atropisomers of 3-aryl-4(3H)-quinazolinones and their use
as AMPA-receptor antagonists
IN Welch, Willard McKowan, Jr.; Devries, Keith M.
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D239-91
ICS C07D401-06; C07D417-06; C07D401-14; C07D405-06; C07D413-06;
A61K031-505; C07M007-00
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9838173	A1	19980903	WO 1998-IB150	19980206
W:				
AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,				
KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,				
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,				
US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,				
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,				
GA, GN, ML, MR, NE, SN, TD, TG				
AU 9856768	A1	19980918	AU 1998-56768	19980206
PRAI US 1997-38905		19970228		
WO 1998-IB150		19980206		
OS MARPAT 129:230733				
GI				



AB Title atropisomers [I; wherein R2 is an optionally substituted aryl or heteroaryl, R5 is alkyl, halo, CF3, alkoxy or alkylthio, R6, R7 and R8 are hydrogen or halo, and R3 is hydrogen, halo, CN, NO2, CF3, alkyl or alkoxy] are prepd. and are useful as AMPA receptor antagonists, particularly in the treatment of neurodegenerative and CNS-trauma related conditions (no data). The title (S)-atropisomer II was prepd. from 2-chloroaniline, 6-fluoro-2-methylquinazolin-4-one which was prepd. from hydrogenation, acetylation, and cyclization of 2-nitro-5-fluorobenzoic acid, followed by reaction with 2,6-pyridinedicarboxaldehyde, and diethylamine, and was column sepd.

ST quinazolinone prepn; atropisomer quinazolinone sepn HPLC receptor antagonist

IT Separation

(HPLC column; prepn. and sepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT AMPA receptors

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(antagonists; prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT 212850-63-0P 212850-64-1P 212850-65-2P 212850-66-3P 212850-68-5P
212850-70-9P 212850-72-1P 212850-73-2P 212850-74-3P 212850-75-4P
212850-76-5P 212850-77-6P 212850-78-7P 212850-79-8P 212850-80-1P
212850-81-2P 212850-82-3P 212916-59-1P 212916-60-4P 212916-61-5P
212916-62-6P 212916-63-7P 212916-64-8P 212916-65-9P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

10 212850-63-0P 212850-64-1P 212850-65-2P 212850-66-3P 212850-68-5P
212850-70-9P 212850-72-1P 212850-73-2P 212850-74-3P 212850-75-4P
212850-76-5P 212850-77-6P 212850-78-7P 212850-79-8P 212850-80-1P
212850-81-2P 212850-82-3P 212916-59-1P 212916-60-4P 212916-61-5P
212916-62-6P 212916-63-7P 212916-64-8P 212916-65-9P

(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT	10200-43-8P	49579-12-6P	68683-04-5P	78441-69-7P	82586-66-1P
	113732-84-6P	141567-53-5P	174608-36-7P	194473-04-6P	199599-68-3P
	199655-35-1P	199655-36-2P	199655-54-4P	199655-55-5P	199655-57-7P
	199655-61-3P	199655-62-4P	199655-63-5P	199655-65-7P	199655-66-8P
	199655-67-9P	199655-68-0P	199655-69-1P	199655-70-4P	199655-71-5P
	199655-72-6P	199655-73-7P	199655-74-8P	199655-75-9P	199655-76-0P
	199655-77-1P	199655-78-2P	199655-79-3P	199655-80-6P	
	199655-81-7P	199655-82-8P	199655-83-9P	199655-84-0P	
	199655-86-2P	199655-87-3P	199655-88-4P	199655-89-5P	199655-90-8P
	199655-91-9P	199655-92-0P	199655-93-1P	199655-96-4P	199655-97-5P
	199655-98-6P	199655-99-7P	199656-02-5P	199656-03-6P	199656-04-7P
	199656-05-8P	199656-06-9P	199656-28-5P	199656-29-6P	199656-30-9P
	199656-31-0P	199656-32-1P	199656-33-2P	199656-34-3P	199656-35-4P
	199656-40-1P	212764-92-6P	212764-93-7P	212764-94-8P	212764-95-9P
	212764-96-0P	212764-97-1P	212764-99-3P	212765-00-9P	212765-01-0P
	212765-02-1P	212765-03-2P	212765-05-4P	212765-06-5P	212765-07-6P
	212765-08-7P	212765-09-8P	212765-10-1P	212765-11-2P	212765-12-3P
	212765-13-4P	212765-15-6P	212765-16-7P	212765-19-0P	212765-20-3P
	212765-21-4P	212765-22-5P	212765-23-6P	212765-24-7P	212765-25-8P
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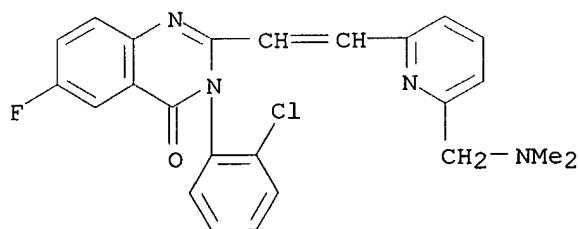
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

IT **199655-81-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of atropisomers of arylquinazolinones as AMPA-receptor antagonists)

RN 199655-81-7 CAPLUS

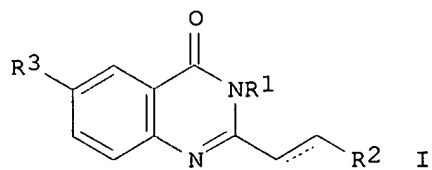
CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d py all hitstr 4

L9 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS
PY 1997
1997
1997
1999
1999
1999
AN 1997:752948 CAPLUS
DN 128:34774
TI Preparation of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists.
IN Elliott, Mark Leonard; Welch, Willard Mckowan Jr
PA Pfizer Inc., USA; Elliott, Mark Leonard; Welch, Willard Mckowan Jr.
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D401-06
ICS C07D401-04; C07D401-14; C07D405-06; C07D403-06; C07D239-91;
C07D417-14; C07D417-06; A61K031-505
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9743276	A1	19971120	WO 1997-IB134	19970217
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2252907	AA	19971120	CA 1997-2252907	19970217
	AU 9715549	A1	19971205	AU 1997-15549	19970217
	EP 901487	A1	19990317	EP 1997-901749	19970217
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
	CN 1218464	A	19990602	CN 1997-194654	19970217
	NO 9805293	A	19990113	NO 1998-5293	19981113
PRAI	US 1996-17738		19960515		
	WO 1997-IB134		19970217		
OS	MARPAT 128:34774				
GI					



AB Title compds. [I; R1 = (substituted) Ph, pyridyl; R2 = (substituted) Ph, 5-6 membered heterocyclyl; R3 = H, halo, cyano, No2, CF3, alkyl, alkoxy], were prepd. Thus, 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylvinyl)-3H-quinazolin-4-one was hydrogenated in EtOAc over Pd/C to give 100% 3-(2-chlorophenyl)-6-fluoro-2-(2-pyridin-2-ylethyl)-3H-quinazolin-4-one. Tested I inhibited AMPA receptor activation-induced 45Ca2+ uptake with IC50 <5 .mu.M.

ST quinazolinone prepn AMPA receptor antagonist; nervous system agents
quinazolinone

IT Nervous system agents
Neurotransmitter antagonists
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT 3257-47-4P 199655-35-1P 199655-36-2P 199655-37-3P 199655-38-4P
199655-39-5P 199655-40-8P 199655-41-9P 199655-42-0P 199655-43-1P
199655-44-2P 199655-45-3P 199655-46-4P 199655-47-5P 199655-48-6P
199655-49-7P 199655-50-0P 199655-51-1P 199655-52-2P 199655-53-3P
199655-54-4P 199655-55-5P 199655-56-6P 199655-57-7P 199655-58-8P
199655-59-9P 199655-60-2P 199655-61-3P 199655-62-4P 199655-63-5P
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199655-74-8P 199655-75-9P 199655-76-0P 199655-77-1P 199655-78-2P
199655-79-3P 199655-80-6P **199655-81-7P** 199655-82-8P
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199655-98-6P 199655-99-7P 199656-00-3P 199656-01-4P 199656-02-5P
199656-03-6P 199656-04-7P 199656-05-8P 199656-06-9P 199656-07-0P
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199656-23-0P 199656-24-1P 199656-25-2P 199656-26-3P 199656-27-4P
199656-28-5P 199656-29-6P 199656-30-9P 199656-31-0P 199656-32-1P
199656-33-2P 199656-34-3P 199656-35-4P 199656-36-5P 199656-37-6P
199656-38-7P 199656-39-8P 199656-40-1P 199656-41-2P 199656-44-5P
199656-45-6P 199656-46-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

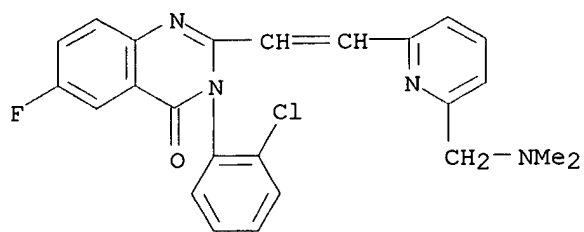
IT 95-51-2, 2-Chloroaniline 320-98-9 340-57-8 5431-44-7,
2,6-Pyridinedicarboxaldehyde 20949-84-2, 2-Methylthiazole-4-
carboxaldehyde 49579-01-3 49579-08-0 199599-68-3 199656-42-3
199656-43-4
RL: RCT (Reactant)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT 38520-78-4P 49579-12-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

IT **199655-81-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,3-disubstituted-4(3H)-quinazolinones as AMPA receptor antagonists)

RN 199655-81-7 CAPLUS

CN 4(3H)-Quinazolinone, 3-(2-chlorophenyl)-2-[2-[6-[(dimethylamino)methyl]-2-pyridinyl]ethenyl]-6-fluoro- (9CI) (CA INDEX NAME)



=> d std bib ab clm

L14 ANSWER 1 OF 1 USPATFULL

AN 97:86624 USPATFULL

TI Excitatory amino acid receptor antagonists

IN Arnold, M. Brian, Franklin, IN, United States

Augenstein, Nancy K., Indianapolis, IN, United States

Lunn, William H. W., Indianapolis, IN, United States

Ornstein, Paul L., Indianapolis, IN, United States

Schoepp, Darryle D., Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5670516 19970923

AI US 1995-456439 19950601 (8)

RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994, now abandoned which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957

DT Utility

LN.CNT 3909

INCL INCLM: 514/307.000

INCLS: 546/147.000

NCL NCLM: 514/307.000

NCLS: 546/147.000

IC [6]

ICM: C07D215-14

ICS: A61K031-47

EXF 546/23; 546/146; 546/147; 546/148; 546/150; 514/307

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 97:86624 USPATFULL

TI Excitatory amino acid receptor antagonists

IN Arnold, M. Brian, Franklin, IN, United States

Augenstein, Nancy K., Indianapolis, IN, United States

Lunn, William H. W., Indianapolis, IN, United States

Ornstein, Paul L., Indianapolis, IN, United States

Schoepp, Darryle D., Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5670516 19970923

AI US 1995-456439 19950601 (8)

RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994, now abandoned which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957

DT Utility

EXNAM Primary Examiner: Davis, Zinna Northington

LREP Hay, Martin A.; Leeds, James P.

CLMN Number of Claims: 42

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3909

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines, as well as, novel intermediates in the synthesis thereof.

CLM What is claimed is:

1. A compound of the formula ##STR87## wherein: R.sup.1 is hydrogen,

C.sub.1 -C.sub.10 alkyl, arylalkyl, alkoxy carbonyl or acyl; R.sup.2 is hydrogen, C.sub.1 -C.sub.6 alkyl, substituted alkyl, cycloalkyl, or arylalkyl; R.sup.3 is CO.sub.2 H, SO.sub.3 H, CONHSO.sub.2 R.sup.8, or a group of formula ##STR88## W is (CH.sub.2).sub.n, S, SO, SO.sub.2 ; Y is CHR.sup.7, NR.sup.4, O, S, SO, or SO.sub.2 ; Z is NR.sup.6, CHR.sup.7, or CH; or W and Y together are HC.dbd.CH or C.tbd.C, or Y and Z together are HC.dbd.CH or C.tbd.C; R.sup.4 is hydrogen, C.sub.1 -C.sub.4 alkyl, phenyl, or acyl; R.sup.5 is hydrogen, C.sub.1 -C.sub.4 alkyl, CF.sub.3, phenyl, hydroxy, amino, bromo, iodo, or chloro; R.sup.6 is acyl; R.sup.7 is independently hydrogen, C.sub.1 -C.sub.4 alkyl, phenyl, or substituted phenyl; R.sup.8 is C.sub.1 -C.sub.4 alkyl or tetrazole-5-yl; and n is 0, 1, or 2; provided that when Y is NR.sup.4, O, S, SO, or SO.sub.2, W is (CH.sub.2).sub.n and Z is CHR.sup.7 or CH; further provided that when W is S, SO, or SO.sub.2, Y is CHR.sup.7, Z is CHR.sup.7 or CH, or Y and Z together are HC.dbd.CH or C.tbd.C; further provided that when W and Z are CH.sub.2, Y is not S; further provided that when W and Y together are HC.dbd.CH or C.tbd.C, Z is CHR.sub.7 ; or a pharmaceutically acceptable salt thereof.

2. A compound of claim 1 wherein: R.sup.1 is hydrogen or alkoxy carbonyl; R.sup.2 is hydrogen or C.sub.1 -C.sub.6 alkyl; R.sup.3 is a group selected from the group consisting of CO.sub.2 H, SO.sub.3 H, CONHSO.sub.2 R.sup.8, and ##STR89## W is S or (CH.sub.2).sub.n ; n is 0, 1, or 2; Y is CHR.sup.7, S, SO.sub.2 or O; Z is CHR.sup.7 or NR.sup.6 ; or Y and Z together are HC.dbd.CH; R.sup.6 is formyl; R.sup.7 is independently hydrogen, C.sub.1 -C.sub.4 alkyl, or phenyl; R.sup.8 is C.sub.1 -C.sub.4 alkyl or tetrazole-5-yl; or a pharmaceutically acceptable salt thereof.

3. A compound of claim 2 wherein R.sup.1 and R.sup.2 are hydrogen, or a pharmaceutically acceptable salt thereof.

4. A compound of claim 2 wherein: R.sup.1 is hydrogen or alkoxy carbonyl; R.sup.2 is hydrogen or C.sub.1 -C.sub.6 alkyl; R.sup.3 is a group selected from the group consisting of SO.sub.3 H and a group of the formula ##STR90## W is S, SO.sub.2 or (CH.sub.2).sub.n ; n is 0, 1, or 2; Y is CHR.sup.7, S, or SO.sub.2 ; Z is CHR.sup.7 ; R.sup.5 is hydrogen, C.sub.1 -C.sub.4 alkyl, or CF.sub.3 ; and R.sup.7 is hydrogen, C.sub.1 -C.sub.4 alkyl, or phenyl; or a pharmaceutically acceptable salt thereof.

5. A compound of claim 4 wherein: R.sup.1 and R.sup.2 are hydrogen, or a pharmaceutically acceptable salt thereof.

6. A compound of claim 4 wherein: R.sup.1 and R.sup.2 are hydrogen; R.sup.3 is a group selected from the group of the formula ##STR91## W is (CH.sub.2).sub.n ; n is 0; Y is CHR.sup.7, S, or SO.sub.2 ; Z is CHR.sup.7 ; R.sup.5 is hydrogen or C.sub.1 -C.sub.4 alkyl; and R.sup.7 is hydrogen, C.sub.1 -C.sub.4 alkyl, or phenyl; or a pharmaceutically acceptable salt thereof.

7. A compound of claim 6 wherein R.sup.3 is a group of the formula ##STR92## or a pharmaceutically acceptable salt thereof.

8. A compound of claim 6 wherein R.sup.3 is a group of the formula ##STR93## or a pharmaceutically acceptable salt thereof.

9. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

10. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
11. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
12. The compound of claim 6 which is (3S,4aR,6S,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
13. The compound of claim 6 which is 6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
14. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
15. The compound of claim 6 which is 6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
16. The compound of claim 6 which is (3S,4aR,6S,8aR)-6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
17. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
18. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
19. The compound of claim 6 which is 6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
20. The compound of claim 6 which is (3S,4aR,6R,8aR)-6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.
21. A method of blocking the **AMPA** excitatory amino acid receptor in mammals which comprises administering to a mammal requiring decreased excitatory amino acid neurotransmission a pharmaceutically-effective amount of a compound of claim 1.
22. A method of blocking the **AMPA** excitatory amino acid receptor in mammals which comprises administering to a mammal requiring decreased excitatory amino acid neurotransmission a pharmaceutically-effective amount of a compound of claim 6.
23. A method of treating a neurological disorder in a patient, which comprises administering to a patient in need thereof, an effective amount of a compound of claim 1.
24. The method of claim 23 wherein said neurological disorder is

cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive dyskinesia.

25. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, cardiac arrest, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, chronic pain, psychosis, emesis, muscular spasms, amyotrophic lateral sclerosis, or ocular damage and retinopathy.

26. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, ocular damage and retinopathy, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, or chronic pain.

27. The method of claim 23 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, or ocular damage and retinopathy.

28. A method of treating a neurological disorder in a patient, which comprises administering to a patient in need thereof, an effective amount of a compound of claim 6.

29. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive dyskinesia.

30. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, cardiac arrest, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, chronic pain, psychosis, emesis, muscular spasms, amyotrophic lateral sclerosis, or ocular damage and retinopathy.

31. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, ocular damage and retinopathy, Alzheimer's Disease, idiopathic and drug-induced Parkinson's Disease, AIDS-induced dementia, convulsions, or chronic pain.

32. The method of claim 28 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, head trauma, spinal cord trauma, cardiac arrest, or ocular damage and retinopathy.

33. A method of producing analgesia in mammals which comprises administering to a mammal an effective amount of a compound of claim 1.

34. A method of producing analgesia in mammals which comprises administering to a mammal an effective amount of a compound of claim 6.

35. A pharmaceutical formulation comprising a compound of claim 1 and a pharmaceutically-acceptable carrier, diluent, or excipient.

36. A pharmaceutical formulation comprising a compound of claim 6 and a pharmaceutically-acceptable carrier, diluent, or excipient.

37. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

38. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-2-thiaethyl]-decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt.

39. A formulation according to claim 36 wherein the compound is 6-[2-(3-hydroxyisoxazole-5-yl)ethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

40. A formulation according to claim 35 wherein the compound is 6-[(1(2-4)H-1,2,4-triazole-5-yl)sulfonylmethyl]-decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

41. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-1-methylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

42. A formulation according to claim 36 wherein the compound is 6-[2-(1(2)H-tetrazole-5-yl)-1-phenylethyl]decahydroisoquinoline-3-carboxylic acid or a pharmaceutically acceptable salt thereof.

=> d 134 std bib ab hit

L34 ANSWER 1 OF 5 USPATFULL

AN 97:16213 USPATFULL

TI Isoquinolinyl-carboxylic acid receptor antagonists compounds

IN Huff, Bret, Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5606062 19970225 <--

AI US 1995-457556 19950601 (8)

RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994 which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957

DT Utility

LN.CNT 3730

INCL INCLM: 546/147.000

NCL NCLM: 546/147.000

IC [6]

ICM: C07D217-16

EXF 546/146; 546/147

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 97:16213 USPATFULL

TI Isoquinolinyl-carboxylic acid receptor antagonists compounds

IN Huff, Bret, Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5606062 19970225 <--

AI US 1995-457556 19950601 (8)

RLI Division of Ser. No. US 1994-343079, filed on 21 Nov 1994 which is a division of Ser. No. US 1993-111747, filed on 25 Aug 1993, now patented, Pat. No. US 5399696 which is a division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented, Pat. No. US 5284957

DT Utility

EXNAM Primary Examiner: Davis, Zinna Northington

LREP Hay, Martin A.; Leeds, James P.

CLMN Number of Claims: 6

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3730

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines, as well as, novel intermediates in the synthesis thereof.

PI US 5606062 19970225 <--

SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of acute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary

incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive **dyskinesia**. The use of a neuroprotective agent, such as an AMPA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The EAA antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to the excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 134 std bib ab hit 2

L34 ANSWER 2 OF 5 USPATFULL

AN 96:53325 USPATFULL

TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists

IN Ornstein, Paul L., Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5527810 19960618 <--

AI US 1994-255590 19940608 (8)

RLI Division of Ser. No. US 1992-972679, filed on 6 Nov 1992, now patented, Pat. No. US 5356902

DT Utility

LN.CNT 1477

INCL INCLM: 514/307.000

INCLS: 546/144.000; 546/147.000

NCL NCLM: 514/307.000

NCLS: 546/144.000; 546/147.000

IC [6]

ICM: A01N043-42

ICS: C07D217-00

EXF 546/144; 546/147; 514/307

AN 96:53325 USPATFULL

TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists

IN Ornstein, Paul L., Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5527810 19960618 <--

AI US 1994-255590 19940608 (8)

RLI Division of Ser. No. US 1992-972679, filed on 6 Nov 1992, now patented, Pat. No. US 5356902

DT Utility

EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Covington, Raymond

LREP Hay, Martin A.; Leeds, James P.

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1477

AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders. This invention also provides synthetic methods for preparing decahydroisoquinolines.

PI US 5527810 19960618 <--

SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of acute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive

dyskinesia. The use of a neuroprotective agent, such as an AMPA or NMDA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The excitatory amino acid antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA or the NMDA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to these excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

CLM What is claimed is:

2. The method of claim 1 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.

7. The method of claim 6 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**.

=> d 134 std bib ab hit 3

L34 ANSWER 3 OF 5 USPATFULL

AN 95:78190 USPATFULL

TI Aryl-spaced decahydroisoquinoline-3-carboxylic acids as excitatory amino acid receptor antagonists

IN Ornstein, Paul L., Carmel, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5446051 19950829 <--

AI US 1994-251809 19940531 (8)

DT Utility

LN.CNT 1093

INCL INCLM: 514/307.000

INCLS: 546/022.000; 546/147.000

NCL NCLM: 514/307.000

NCLS: 546/022.000; 546/147.000

IC [6]

ICM: C07D217-06

ICS: A61K031-47

EXF 546/22; 546/146; 546/147; 514/307

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 95:78190 USPATFULL

TI Aryl-spaced decahydroisoquinoline-3-carboxylic acids as excitatory amino acid receptor antagonists

IN Ornstein, Paul L., Carmel, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5446051 19950829 <--

AI US 1994-251809 19940531 (8)

DT Utility

EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Davis, Zinna N.

LREP Hay, Martin A.; Dodd, Thomas J.; Boone, David E.

CLMN Number of Claims: 40

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1093

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides novel decahydroisoquinoline derivatives which are useful as excitatory amino acid antagonists. The invention also provides for methods of using these derivatives to treat various neurological disorders.

PI US 5446051 19950829 <--

SUMM Use of Formula (I) compounds as AMPA selective antagonists is seen as potentially beneficial in treating a number of neurodegenerative conditions including, but not limited to Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, cognitive disorders, Parkinson's Disease, anxiety, emesis, brain edema, chronic pain and tardive **dyskinesia**, among others. Formula (I) compounds are also contemplated for use to abate cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, and spinal cord and brain trauma injuries. Further, Formula (I) compounds are contemplated for use as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to

have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 134 std bib ab hit 4

L34 ANSWER 4 OF 5 USPATFULL

AN 95:25041 USPATFULL
TI Isoquinolinyl compounds which are intermediates
IN Arnold, M. Brian, Franklin, IN, United States
Augenstein, Nancy K., Indianapolis, IN, United States
Lunn, William H. W., Indianapolis, IN, United States
Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.
corporation)
PI US 5399696 19950321 <--
AI US 1993-111747 19930825 (8)
RLI Division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented,
Pat. No. US 5284957
DT Utility
LN.CNT 3727
INCL INCLM: 546/147.000
NCL NCLM: 546/147.000
IC [6]
ICM: C07D217-02

EXF 546/147; 546/15

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AN 95:25041 USPATFULL
TI Isoquinolinyl compounds which are intermediates
IN Arnold, M. Brian, Franklin, IN, United States
Augenstein, Nancy K., Indianapolis, IN, United States
Lunn, William H. W., Indianapolis, IN, United States
Ornstein, Paul L., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.
corporation)
PI US 5399696 19950321 <--
AI US 1993-111747 19930825 (8)
RLI Division of Ser. No. US 1992-939780, filed on 3 Sep 1992, now patented,
Pat. No. US 5284957
DT Utility
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Davis, Zinna N.
LREP Leeds, James P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3727

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides novel decahydroisoquinoline compounds which are
useful as excitatory amino acid receptor antagonists and in the
treatment of neurological disorders. This invention also provides
synthetic methods for preparing decahydroisoquinolines, as well as,
novel intermediates in the synthesis thereof.

PI US 5399696 19950321 <--
SUMM Excitatory amino acid excitotoxicity has been implicated in the
pathophysiology of a number of neurological disorders. This
excitotoxicity has been implicated in the pathophysiology of acute and
chronic neurodegenerative conditions including cerebral deficits
subsequent to cardiac bypass surgery and grafting, stroke, cerebral
ischemia, spinal cord trauma, head trauma, Alzheimer's Disease,
Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced
dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal
damage, ocular damage and retinopathy, and idiopathic and drug-induced
Parkinson's Disease. Other neurological conditions, that are caused by

glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive dyskinesia. The use of a neuroprotective agent, such as an AMPA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The EAA antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to the excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive dyskinesia. The formula I compounds are also useful as analgesic agents.

SUMM The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive dyskinesia. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

=> d 134 std bib ab hit 5

L34 ANSWER 5 OF 5 USPATFULL

AN 94:91059 USPATFULL

TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists

IN Ornstein, Paul L., Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5356902 19941018 <--

AI US 1992-972679 19921106 (7)

DT Utility

LN.CNT 1383

INCL INCLM: 514/307.000

INCLS: 546/144.000; 546/147.000

NCL NCLM: 514/307.000

NCLS: 546/144.000; 546/147.000

IC [5]

ICM: A01N043-42

ICS: C07D217-00

EXF 546/147; 546/144; 514/307

AN 94:91059 USPATFULL

TI Decahydroisoquinoline compounds as excitatory amino acid receptor antagonists

IN Ornstein, Paul L., Indianapolis, IN, United States

PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5356902 19941018 <--

AI US 1992-972679 19921106 (7)

DT Utility

EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Covington, Raymond

LREP Leeds, James P.

CLMN Number of Claims: 16

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1383

AB This invention provides novel decahydroisoquinoline compounds which are useful as excitatory amino acid receptor antagonists and in the treatment of neurological disorders.

PI US 5356902 19941018 <--

SUMM Excitatory amino acid excitotoxicity has been implicated in the pathophysiology of a number of neurological disorders. This excitotoxicity has been implicated in the pathophysiology of a cute and chronic neurodegenerative conditions including cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, ocular damage and retinopathy, and idiopathic and drug-induced Parkinson's Disease. Other neurological conditions, that are caused by glutamate dysfunction, require neuromodulation. These other neurological conditions include muscular spasms, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, convulsions, and tardive dyskinesia. The use of a neuroprotective agent, such as an AMPA or NMDA receptor antagonist, is believed to be useful in treating these disorders and/or reducing the amount of neurological damage associated with these disorders. The excitatory amino acid antagonists are also useful as analgesic agents.

SUMM Further embodiments of the invention include a method of blocking the AMPA or the NMDA excitatory amino acid receptor, as well as methods of treating a neurological disorder which has been linked to these excitatory amino acid receptors, which comprises administering a compound of formula I. Examples of such neurological disorders which are treated with a formula I compound include cerebral deficits subsequent to cardiac bypass surgery and grafting, stroke, cerebral ischemia, spinal cord trauma, head trauma, Alzheimer's Disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, muscular spasms, migraine headaches, urinary incontinence, psychosis, convulsions, perinatal hypoxia, cardiac arrest, hypoglycemic neuronal damage, opiate tolerance and withdrawal, ocular damage and retinopathy, idiopathic and drug-induced Parkinson's Disease, anxiety, emesis, brain edema, chronic pain, or tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents.

DETD The formula I compounds of the present invention are also believed to have the ability to treat a variety of other neurological disorders in mammals that are associated with glutamate dysfunction including muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, opiate tolerance and withdrawal, anxiety, emesis, brain edema, chronic pain, and tardive **dyskinesia**. The formula I compounds are also useful as analgesic agents. Therefore, the present invention also provides methods for treating these disorders which comprise administering to a patient in need thereof an effective amount of a compound of formula I.

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L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 1999 ACS

PY 1996
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AN 1996:307308 CAPLUS

DN 124:343338

TI Physical form of dihydro-2,3-benzodiazepine derivative useful as an
AMPA antagonist

IN Anderson, Benjamin Alan; Hansen, Marvin Martin; Vicenzi, Jeffrey Thomas;
Varie, David Lee; Zmijewski, Milton Joseph, Jr.; Harkness, Allen Robert

PA Lilly, Eli, and Co., USA

SO Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DT Patent

LA English

IC ICM C07D491-056

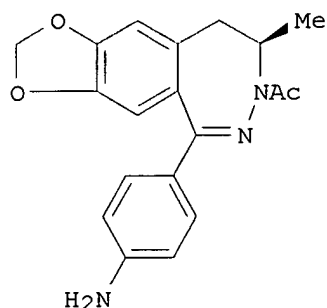
ICS A61K031-55

ICI C07D491-056, C07D317-00, C07D243-00

CC 28-21 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 16, 63

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 699676	A1	19960306	EP 1995-306048	19950830
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, MC, NL, PT, SE				
	NO 9503395	A	19960301	NO 1995-3395	19950830
	CA 2157247	AA	19960301	CA 1995-2157247	19950830
	FI 9504065	A	19960301	FI 1995-4065	19950830
	AU 9530356	A1	19960314	AU 1995-30356	19950830
	AU 696243	B2	19980903		
	JP 08092255	A2	19960409	JP 1995-221572	19950830
	CN 1122338	A	19960515	CN 1995-109526	19950830
	HU 72673	A2	19960528	HU 1995-2547	19950830
	BR 9503844	A	19960910	BR 1995-3844	19950830
	IL 115101	A1	19981227	IL 1995-115101	19950830
PRAI	US 1994-298645	19940831			
	US 1995-413024	19950328			
	US 1994-289645	19940831			
OS	CASREACT 124:343338				
GI					



- AB A phys. form of (R)-7-acetyl-5-(4-aminophenyl)-8,9-dihydro-8-methyl-7H-1,3-dioxolo[4,5-h][2,3]benzodiazepine (I) is disclosed, having an x-ray powder diffraction pattern with d spacings at 10.61, 8.83, 6.78, 5.83, 4.13 and 3.74 .ANG.. The compd. is an **AMPA antagonist** (no data), useful for treating a variety of CNS and other disorders. I is prepd. in approx. 7 steps with several variations. For example, reductive fermn. of (3,4-methylenedioxyphenyl)acetone with *Zygosaccharomyces rouxii* ATCC 14462 gave (S)-.alpha.-methyl-1,3-benzodioxole-5-ethanol in 85-90% isolated yield and 100% ee. This underwent cyclization with p-nitrobenzaldehyde to a benzopyran deriv. (87-93%), atm. hydroxylation in DMSO-DMF to a cyclic hemiacetal, ring cleavage by AcNHNH₂ to an alc./hydrazone (91%), mesylation of the alc. (87%), cyclization of the mesylate/hydrazone (90%), and redn. of the nitro group with aq. K formate over Pd/C (93%), giving form IV of I. Two chem. variants of the 1st step, and prepn. of forms I, II, and III of I using different redn. procedures in the last step, are also described.
- ST benzodiazepine prepn **AMPA antagonist**;
dioxolobenzodiazepine acetylaminophenyldihydromethyl form IV prepn
- IT Analgesics
Anticonvulsants and Antiepileptics
Antiemetics
Anxiolytics
Muscle relaxants
Nervous system agents
(prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT *Saccharomyces rouxii*
(reductive fermn. of (methylenedioxyphenyl)acetone; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Drug dependence
Parkinsonism
(treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Mental disorder
(Alzheimer's disease, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Tranquilizers and Neuroleptics
(antipsychotics, prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Mental disorder
(dementia, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor antagonist**)
- IT Nervous system
(disease, Huntington's chorea, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA receptor**

antagonist)
 IT Nervous system
 (disease, amyotrophic lateral sclerosis, treatment; prepn. of
 dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor
 antagonist)
 IT Bladder
 (disease, incontinence, treatment; prepn. of dihydro-2,3-benzodiazepine
 deriv. phys. form as **AMPA** receptor antagonist)
 IT Nervous system
 (disease, tardive **dyskinesia**, treatment; prepn. of
 dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA** receptor
 antagonist)
 IT Brain, disease
 (edema, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys.
 form as **AMPA** receptor antagonist)
 IT Neurotransmitter antagonists
 (glutamatergic, prepn. of dihydro-2,3-benzodiazepine deriv. phys. form
 as **AMPA** receptor antagonist)
 IT Receptors
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
 (Biological study)
 (glutamatergic, AMPA-binding, prepn. of dihydro-2,3-benzodiazepine
 deriv. phys. form as **AMPA** receptor antagonist)
 IT Eye, disease
 (injury, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys.
 form as **AMPA** receptor antagonist)
 IT Brain, disease
 (ischemia, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys.
 form as **AMPA** receptor antagonist)
 IT Headache
 (migraine, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys.
 form as **AMPA** receptor antagonist)
 IT Eye, disease
 (retinopathy, treatment; prepn. of dihydro-2,3-benzodiazepine deriv.
 phys. form as **AMPA** receptor antagonist)
 IT Brain, disease
 (stroke, treatment; prepn. of dihydro-2,3-benzodiazepine deriv. phys.
 form as **AMPA** receptor antagonist)
 IT 172542-26-6P, (S)-.alpha.-Methyl-1,3-benzodioxole-5-ethanol
 RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF
 (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation);
 BIOL (Biological study); PREP (Preparation)
 (intermediate; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form
 as **AMPA** receptor antagonist)
 IT 161832-64-0P 172542-27-7P 172542-28-8P 172542-29-9P 172542-30-2P
 172542-31-3P 172721-25-4P 172721-26-5P 172721-27-6P 176777-96-1P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
 preparation); PREP (Preparation)
 (intermediate; prepn. of dihydro-2,3-benzodiazepine deriv. phys. form
 as **AMPA** receptor antagonist)
 IT 161832-65-1P
 RL: BAC (Biological activity or effector, except adverse); IMF (Industrial
 manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL
 (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of dihydro-2,3-benzodiazepine deriv. phys. form as **AMPA**
 receptor antagonist)
 IT 124-63-0, Methanesulfonyl chloride 555-16-8, p-Nitrobenzaldehyde,
 reactions 1068-57-1, Acetic hydrazide 2635-13-4, 4-Bromo-1,2-
 methylenedioxybenzene 4676-39-5, (3,4-Methylenedioxyphenyl)acetone
 16088-62-3, (S)-(-)-Propylene oxide, reactions

RL: RCT (Reactant)

(starting material; prepn. of dihydro-2,3-benzodiazepine deriv. phys.
form as **AMPA** receptor **antagonist**)